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PLEOMORPHISM AND VARIATION IN THE DERMATOPHYTES

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The identification of species of fungi isolated from ringworm is of importance to the dermatologist. In some instances it suggests the source of infection. There is also evidence that the great variations in the disease picture depend in part on the variety of parasite concerned.

In the differentiation of species emphasis has been laid on the form or color of the giant colony or on the presence or abundance of such structures as fuseaux, spiral hyphae and nodular organs. This has led to the setting up of many species. Brumpt in his last edition of the "Précis de parasitologie" listed seventy-nine. Even so, it is often difficult to identify freshly isolated strains with any one of them.

Sabouraud was able to demonstrate that certain species were parasites of one or another domestic animal, and that human infection with a particular dermatophyte often occurred from one animal. He also showed that certain species differed in virulence. It is, however, by no means clear that all of the numerous species described differ from one another in the hosts to which they are adapted or in the disease picture that they produce; nor does it seem certain that the characteristics on which the species are based are always constant in a given strain.

Certain ascomycetes and Fungi imperfecti that appear botanically related to the parasites of ringworm seem somewhat unstable in their morphology. A strain developed from a single spore, called by Brierley an "isolate," may show abrupt changes in the appearance of colonies or in the production of conidia and characteristic hyphal structures. Such changes are referred to by some authors as mutations and by others as saltations. There is some doubt as to whether they are identical in nature with the mutations observed in higher organisms. Their occurrence and significance will be discussed later.

The new characters usually develop in one part of a colony, and as it grows this area often takes the form of a sector. The occurrence of so-called pleomorphism in these fungi, although it does not usually appear as a sector, is probably one example of such a mutation, and the development of colorless sectors in Trichophyton violaceum is another

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familiar example. De Beurmann and Gougerot called attention to similar changes that are often seen in cultures of Sporotrichum.

In the following report variations will be described that occurred in four strains of dermatophytes. In two of the cases the variants arose in cultures that had been derived from single spores. The variants differed so strikingly in their appearance that, according to the criteria commonly accepted, they would probably be classed as separate species if obtained from separate sources. The occurrence of such variants throws considerable doubt on the validity of the present differentiation of species and makes a revision of our classification of these fungi seem highly important.

The first strain to be discussed is a strain of Achorion gypseum Bodin received from Dr. Sabouraud. This fungus is not a common pathogen in this country, although it has been isolated once in the Laboratory for Medical Mycology of Columbia University. Sabouraud [1] discussed it as an animal Microsporum, and Guiart and Grigorákis [2] have removed it to this genus. The strain I with which this report deals is one of the many monospore strains used in a previous study of the nature of the two types of spores formed. In that investigation [3] it was shown that in A. gypseum and in Trichophyton gypseum cultures from the microconidia or aleuries and those from macroconidia or fuseaux are identical. This observation has been confirmed by Spring [4] for T. interdigitalis. The present study has established the further interesting fact that when a variation from the parent type has occurred both types of spores bear the new characters.

Strain I arose from a single microconidium of Achorion gypseum. A flask culture of this strain on horn had been set away at room temperature for four months. At that time it was observed that there were spots of aberrant growth. Mass transfers of spores from different areas yielded several abnormal types of growth. Photographs of these first transfers appear in figure 1. They may be compared with a photograph of a normal culture of the fungus shown in figure *2, 1.* All cultures shown were grown on Sabouraud's maltose agar medium. It is apparent from the shapes and points of origin of the sectors that some change in the genetic constitution of some of the spores had occurred. Whether this change was induced by the unusual substrate

1. Sabouraud, R.: Généralités concernant les dermatophytes, Ann. de dermat. et syph. **9**:656, 1928.

2. Guiart, J., and Grigorákis, L.: La classification botanique des champignons des teignes, Lyon méd. **141**:369, 1928.

3. Emmons, C. W.: Observations on Achorion Gypseum, Mycologia **23**:87, 1931.

4. Spring, D.: Heterothallism Among the Dermatophytes, Arch. Dermat. & Syph. **24**:22 (July) 1931.

used or whether it was due to the age of the culture is not apparent. It is an important point that the parent strain from which these variants arose grew from a single microconidium or aleurie which was presumably uninucleate. The hyphae and macroconidia or fuseaux of A. gypseum are multinucleate, but the microconidia are usually uninucleate.[5] It is also interesting that this particular strain, as well as other strains isolated in the same series of cultures, had up to this time been quite stable. At this time it gave rise to several new types. Apparently the fungus was in a state of flux such as Das Gupta[6] described for a strain of Cytosporina which he studied.

From the various areas on the plate cultures shown in figure 1, ninety-six monospore cultures were secured. Equal numbers of the two types of spores were used. The monospore cultures exactly reproduced the type of growth from which the respective spores were taken, and the microconidia and macroconidia from a given region gave identical cultures. When sectors appeared in the cultures of the variants, monospore cultures were again made from these sectors. Both types of spores were used, and usually at least ten monospore cultures were made from each type of sector.

Photographs of monospore cultures representing five of the six types of variants are shown in figure 2. A photograph of the parent type is included for comparison. The variants will be described as they appeared in these colonies after growth for two weeks at the temperature of the room on Sabouraud's maltose agar medium. No important differences occur as the cultures age except that in most of the strains the colors fade, and in some strains the macroconidia germinate and produce many microconidia.

Variant A (fig. 2, *2*) is tilleul buff[7] at the center, with a surrounding area of pale olive buff and a light pinkish-cinnamon border. The colony is raised in the center; the surface is feltlike and is marked by irregular radial folds, and the growth is thick. The margin is fimbriate. As the culture ages it assumes lilac tints. This is one of the variants in which further variations have occurred. Two of these further changes are shown in figure 3, *2* and *3*. One of them, the sector marked *a* in figure 3, *2*, resembles variant B. The second, appearing at the periphery of the culture shown in figure 3, *3*, is a reversion to the parent type, strain I. When single spore isolations were made from the finger-

5. Grigorákis, L.: Dermatophytes et Dermatomycoses, Ann. de dermat. et syph. **10**:18, 1929.

6. Das Gupta, S. N.: Studies in the Genera Cytosporina, Phomopsis, and Diaporthe. II. On the Occurrence of Saltation in Cytosporina and Diaporthe, Ann. Bot. **44**:349, 1930.

7. The colors named in these descriptions are those given in Ridgway, R.: Color Standards and Color Nomenclature, Washington, D. C., the Author, 1912.

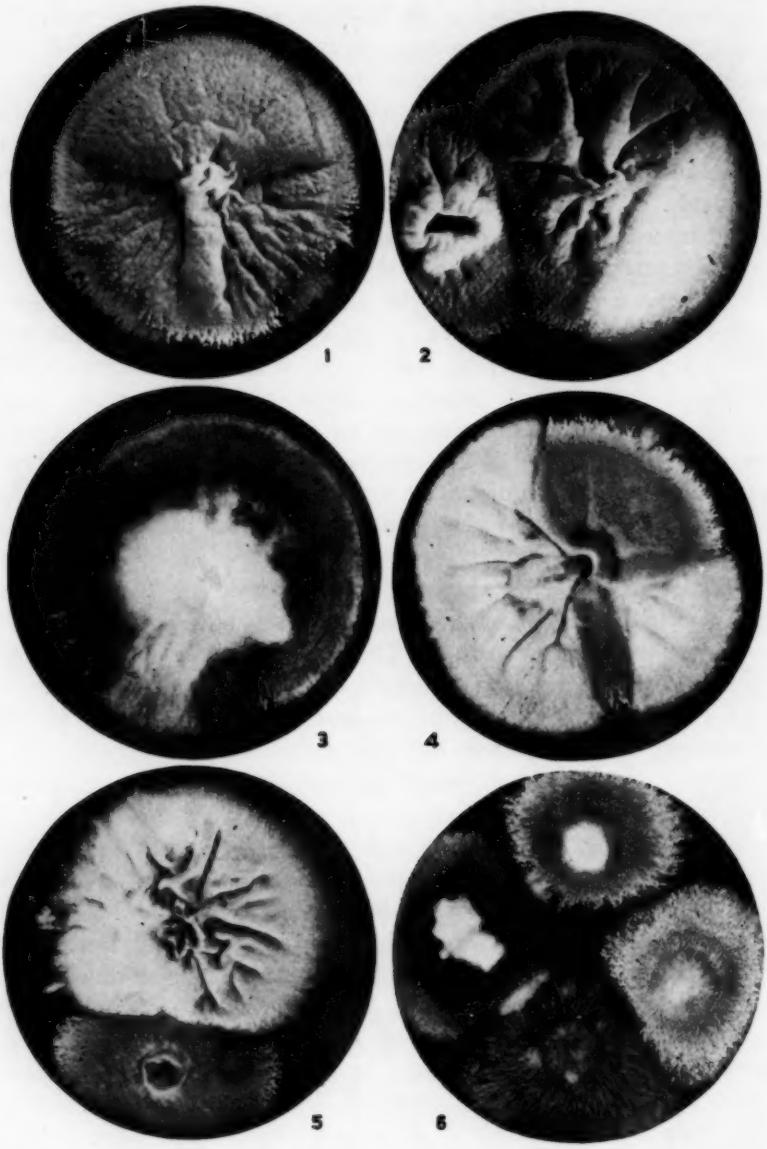

Fig. 1.—Variants of strain I of Achorion gypseum: *1*, mass transfer from flask culture which gave variant A; *2*, mass transfer which gave variants A and B; *3*, mass transfer which gave variants C and F; *4*, mass transfer which gave variants C and D; *5*, mass transfer which gave variants D and E, and *6*, cultures of four strains of A. gypseum.

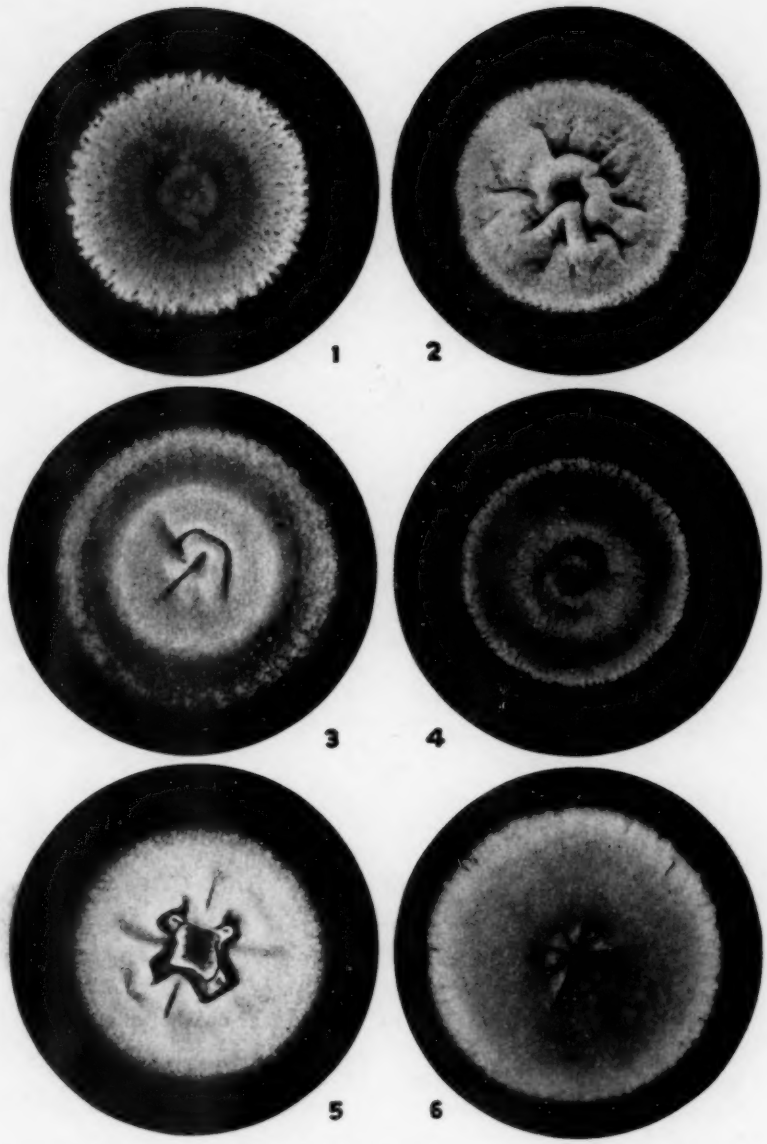

Fig. 2.—Variants of strain I of Achorion gypseum: *1*, normal culture of strain I of A. gypseum; *2*, monospore culture of variant A; *3*, monospore culture of variant C; *4*, monospore culture of variant D; *5*, monospore culture of variant E, and *6*, monospore culture of variant F.

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like projections that terminate the variant A type of growth, some of the microconidia and some of the macroconidia gave colonies like variant A. Others exhibited reversion to type by producing cultures like the original monospore strain I. This reversion will be referred to again. Some subcultures of variant A produce a smooth raised dome instead of the usual radial folds. This is a transient character and is not considered significant. The microscopic appearance of variant A is given in figure 5, *2*. It may be compared with the appearance of the spores of the normal type that are shown in figure 5, *1*. The macroconidia are blunt and have few cells. Many contain one or more dead and empty cells. Whereas in the normal culture the protoplasm is almost totally exhausted in the production of macroconidia, in variant A there is less abundant spore production, and hence there is a great deal of mycelial débris. As in the normal type, there are relatively few microconidia. Spores for this and the following photomicrographs were taken from the older portions of the cultures, because the departures from the normal are more marked than in the younger parts.

Variant B (fig. 2, *3*) has a pinkish-buff center surrounded by a zone of pale pinkish buff and a white periphery. A crater is formed at the center which may be incomplete, as it is in the culture photographed. The surface is composed of an abundant woolly aerial mycelium which extends to the periphery of the colony. Figure 5, *3*, shows the type of spores borne in the culture. All gradations in size between macroconidia and microconidia can be found. There are numerous microconidia. There is considerable development of fine mycelium, and the abundance of the microconidia seems to be due in part at least to the precocious germination of the macroconidia, which gives rise to hyphae which bear the former type. No further variations were observed in this strain.

Variant C is shown in figure 3, *1*. It does not show marked zones of color but is cartridge buff throughout. A slight depression develops at the center of some colonies. There is an abundant development of woolly aerial hyphae, which decreases in depth toward the periphery and covers a more or less granular growth toward the center. Microscopically this strain is like variant B.

Variant D (fig. 2, *4*) is avellaneous at the center. This region is surrounded by a zone of pinkish buff becoming light buff at the margin which is fimbriate. There is a small raised point at the center at the bottom of a very shallow crater. The colony is nearly flat and thin with a granular surface. The character of the spores is shown in figure 5, *4*. This strain produces sectors that are reversions to the original type. Figure 3, *4*, shows a colony from a single microconidium, and figure 3, *5*, one from a single macroconidium, both of which have pro-

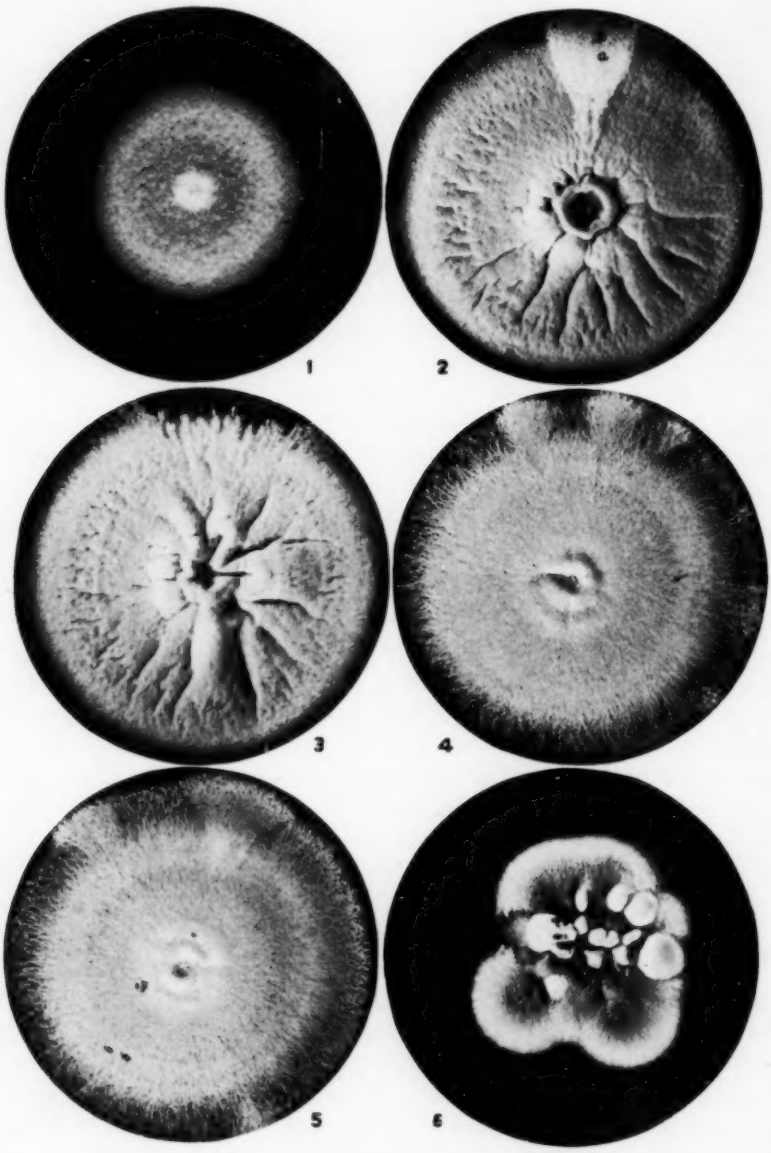

Fig. 3.—Variants of strain I of Achorion gypseum: *1*, variant B of strain I; *2*, variation in monospore culture of variant A; *3*, reversion in monospore culture of variant A; *4*, reversion in culture of variant D from a single microconidium; *5*, reversion in culture of variant D from a single macroconidium, and *6*, culture resulting from an inoculation with a suspension of the spores of variants A to F.

duced several sectors resembling the normal type, as was shown by examination and subculture. This furnishes additional evidence for the identical inheritance, despite their differences in amount of nucleoplasm and cytoplasm, of the two types of spores. The macroconidia, as shown in figure 5, *4*, are very irregular in size and shape. This is in a large part due to the fact that there are so many dead cells in the macroconidia. This results in fragmentation of the spores until they resemble in many cases chlamydospores. There is a great deal of mycelial débris. There are few microconidia.

Variant E (fig. 2, *5*) is cartridge buff throughout, but is paler at the periphery of the colony. A four-sided crater, within which the surface is checked and cracked, forms at the center. There is a depressed furrow just outside the crater, and beyond this there are some shallow radial folds. Growth thins out at the margin. The surface is somewhat powdery. The spores are shown in figure 5, *5*. The macroconidia vary greatly in size. There are few microconidia but an abundance of mycelium.

Variant F (fig. 2, *6*) is chamois or cream buff to cartridge buff or white at the margin. The colony is flat with symmetrical shallow radial furrows. The margin is quite even. The surface is leathery in appearance, but becomes dry and granular with age. The spores (fig. 5, *6*) are nearly normal in appearance.

It should be noted that further variations in the variant strains have in most cases been reversions to the parent type. Except for these occasional variations manifested by sectors, the variant strains have remained constant. Their stability has been tested through twelve generations. They do not become "pleomorphic," i.e., they do not become overgrown with a white, more or less sterile overgrowth. This white duvet which appears in the parent strain is shown clearly at the centers of two of the colonies photographed in figure 1, *6*. In the original strain, I, it usually appears within two weeks on maltose agar at room temperature. Transfers from this growth yield a culture that is by no means sterile, but in which there is a larger proportion of microconidia. Tube cultures of variants kept at room temperature for eight months have not become "pleomorphic." The pleomorphic change, on the other hand, is one that many of the dermatophytes undergo. The dermatophytes appear in this respect to be like the "ever-saltating" strain of Diaporthe described by Horne and Das Gupta.[8] There is a closer parallel, however, in the behavior of certain plant pathogens which must be frequently transferred in order to maintain their fertility and virulence.

8. Horne, A. S., and Das Gupta, S. N.: Studies in the Genera Cytosporina, Phomopsis, and Diaporthe: I. On the Occurrence of an "Ever Saltating" Strain of Diaporthe, Ann. Bot. **43**:417, 1929.

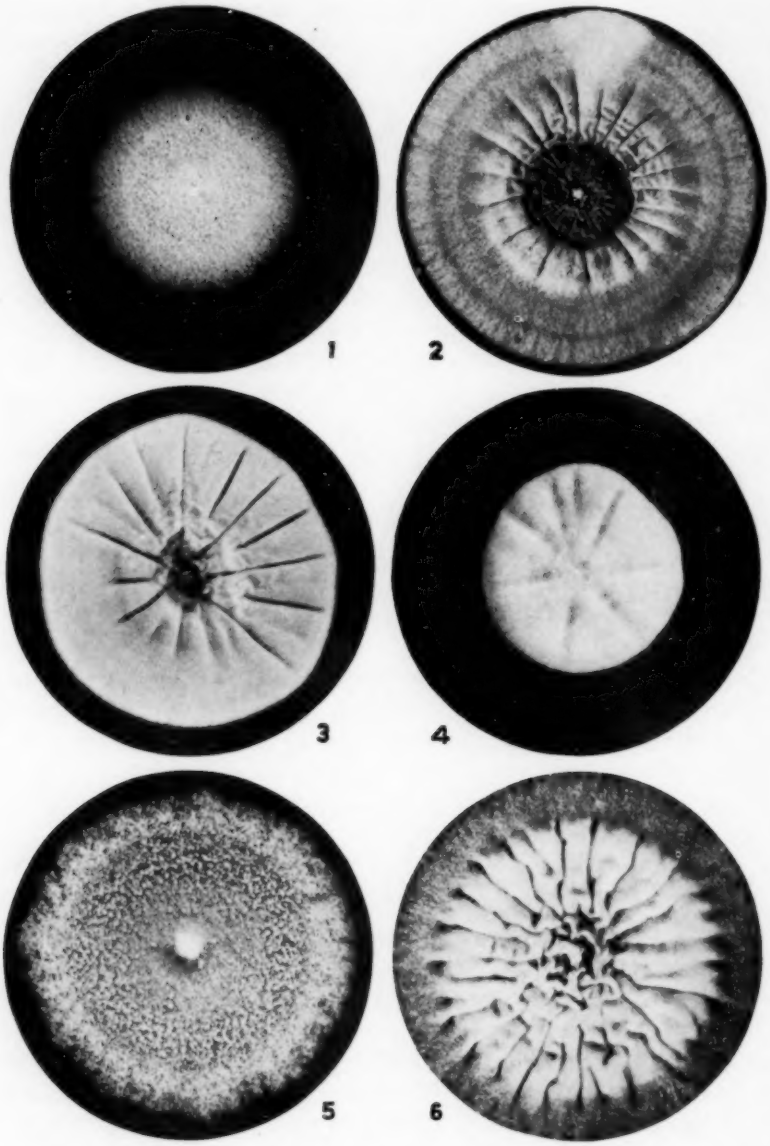

Fig. 4.—Strains III and IV and variants of Trichophyton gypseum: *1*, culture of strain III; *2*, monospore culture of variant M; *3*, variant N; *4*, variant O; *5*, strain IV (Trichophyton gypseum-lacticolor), and *6*, monospore culture of variant W.

The sudden appearance of six variants distinct from the parent and from each other in a single old culture of Achorion gypseum suggested the possibility of contamination by other fungi. This possibility is easily ruled out. The flask had not been repeatedly opened, and there seemed to be little chance for contamination. The variants were unlike any other fungi in this laboratory, nor did they correspond in cultural characteristics to descriptions of any known species. Furthermore, they were sufficiently alike microscopically to show their relationship to the parent species, and in several instances pure cultures of the variants from single spores reverted to the original type. This species, A. gypseum, is itself a variable one so far as we may judge from a study of four strains in our collection. These strains are shown in figure 1, *6*. Three of them came from Dr. Sabouraud's laboratory. While they differ less than do some of the variants, they show marked differences which are constant in culture.

In the hope of obtaining some genetic solution of the origin of these variants, various crossing experiments were attempted. Transfers of certain of the mutants were made at various distances and in various combinations on plates. Spore suspensions containing spores from all the strains were made and put on plates in both heavy and light sowings. One culture resulting from such a sowing is shown in figure 3, *6*. In a few cases variant A showed a tendency to produce the finger-like growth shown in figure 3, *3*, and to revert to type along the line of contact with other variants. This tendency is especially strong when it is grown in proximity to variant F. Since it does this in pure cultures as well, and since other variants did not exhibit the same tendency, no conclusions could be drawn. In no case was there evidence of hybridization. Each type of growth was usually distinct from its neighbor, and often those that grew more rapidly almost obscured those more slow to develop. In cases in which there was any appearance suggesting a myxochimera transfers were made from such a region. In all cases it was possible to isolate the more rapidly growing of the two and to separate both in pure culture if one was not too dominant. There was no evidence of a myxochimera.

Besides the variants described in the foregoing paragraphs, equally striking ones have been observed and selected in three strains of Trichophyton gypseum. One of these, strain II, appeared in one of the monospore cultures of a strain of T. gypseum isolated from a case of trichophytosis of the feet and used in the previously mentioned investigation [3] into the genetic nature of microconidia and macroconidia. In a plate culture of this strain a somewhat "pleomorphic" variant appeared as a narrow white sector originating at the center and running out to the periphery. No extended study was made of it.

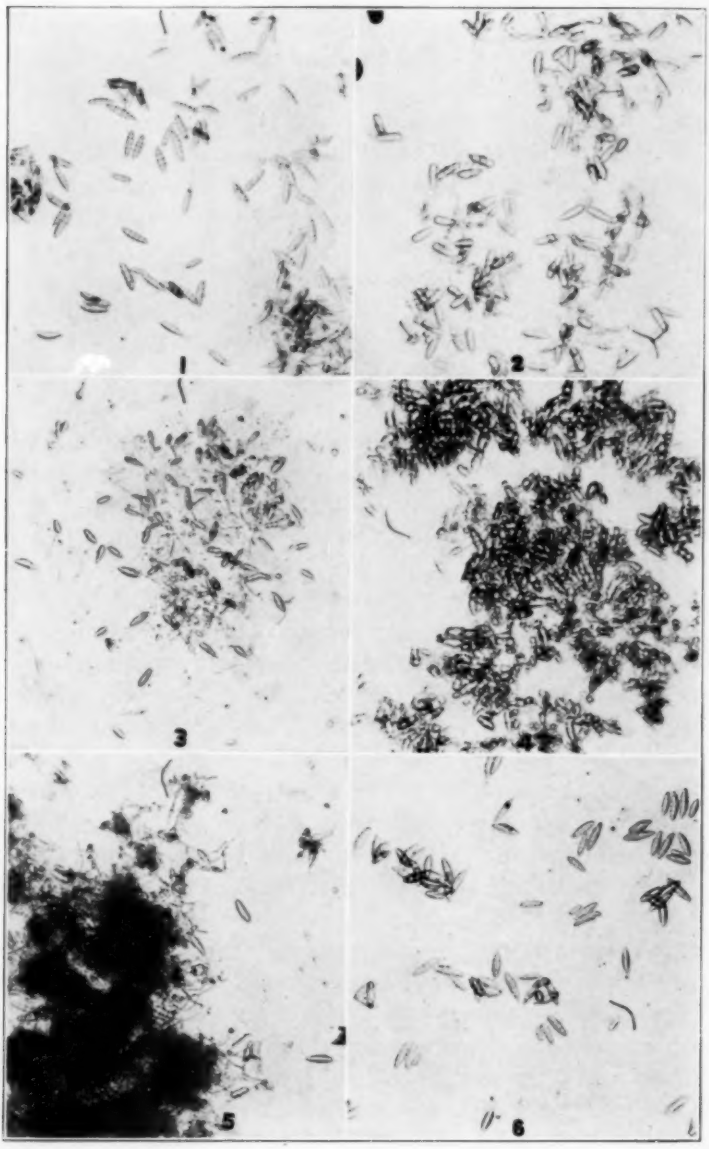

Fig. 5.—Spores of strain I and its variants: *1*, spores of strain I; *2*, spores of variant A; *3*, spores of variant C; *4*, spores of variant D; *5*, spores of variant E, and *6*, spores of variant F.

Strain III was isolated from lesions on the face and neck of a child. Although clearly belonging to the gypseum group, it is an atypical strain, and its unusual features have recommended it for special study. It produces on maltose agar a white, sparse, powdery growth with little aerial mycelium and with the hyphae at the periphery often oriented in a clockwise direction (fig. 4, *1*). The fungus produces microconidia and macroconidia, nodular organs and some spiral hyphae. On a plate culture of this strain that had been exposed to ultraviolet rays a few nodules of deeply pigmented growth developed. Transfers from these points gave cultures of the type shown in figure 4, *2*. This is a photograph of one of several monospore cultures secured, all of which were identical. This variant (M) differs in the character of its surface and pigmentation. The parent type has always produced considerable pigment visible on the reverse side of the colony. On maltose and honey agars the reverse of the colony has been deeply colored in vinaceous tints. In the variant M, this color is also visible on the upper surface of the colony. The surface is wrinkled at the center and there are symmetrical radial folds. In some subcultures of this variant great numbers of long slender macroconidia have been produced.

Variant N (fig. 4, *3*) arose as a yellow sector from M (fig. 4, *2*). It resembles M somewhat in surface, but the radial folds run nearly to the edge. The color is cartridge buff, in marked contrast with strain M, and the reverse is colorless. The microscopic appearance is not significantly different from that of variant O. The other barely noticeable sector appearing in the photograph of M produced a culture essentially like that of M.

Variant O (fig. 4, *4*) is interesting because of its peculiar morphology. It arose on a blood agar slant. It is white with abundant rather soft cottony aerial growth. The texture of the culture is tough, but the hyphae on the surface are unusually fragile, as one may observe in mounting some of the material for microscopic study. The surface is marked by shallow radial furrows. Microscopic examination of a young culture shows abundant conidiophores with partially formed microconidia. These conidia never mature and are not shed. The conidiophore continues to form these abortive conida, but seems unable to store food in them and cut them off. Finally the whole mass forms a clump suggestive of a "nodular organ" if one is unfamiliar with its method of origin and development. The mycelium is of normal diameter and in this respect differs from the fine mycelium of a "pleomorphic" growth.

The last variant (W) to be described developed from strain IV, one of T. gypseum lacticolor from Dr. Sabouraud. This strain, illustrated in figure 4, *5*, remained constant in character for at least two years, but

in a plate culture exposed to ultraviolet rays points of abnormal growth appeared. Transfers from these points gave colonies appearing as in fig. 4, *6*. This is a photograph of one of several identical monospore cultures. The culture varies from white to cream. The parent colony has a granular surface due to the production of great numbers of spores. The variant produces somewhat fewer spores and spirals but more nodular organs.

COMMENT

It is striking that pleomorphism occurred readily in the parent type of Achorion gypseum, but the variants are apparently not subject to this change. When a variant reverts by sector to the parent type, this second variant again becomes liable to the pleomorphic change. I can merely record these observations without attempting any explanation of them.

The factors that induce these variations remain unknown. The variants of Achorion gypseum arose in an old culture on horn. Probably the age and the unusual substrate both played parts in causing them. Other variants differing only slightly from those described have since been isolated from the same flask. Exposure to ultraviolet rays may have induced variation in the cases in which it was followed by a change in the type of culture, but it did not induce such changes in many other plate cultures exposed in the same way. The cytologic features of these fungi may be of significance in this connection. The cells, as was previously noted, are multinucleate. The behavior of these nuclei during growth and cell division is wholly unknown. There is ample opportunity for abnormalities in division during the many vegetative mitoses that must occur.

Variation in other fungi and in bacteria has long been a subject for observation and study. Brierley [9] has made a comprehensive review of the literature on this subject. He suggested a classification of variations emphasizing genetic interpretations and based on type, frequency and permanence. His interpretation of the data recorded by others and of his own observations was that most of the so-called mutations are not mutations in the sense of Jones: [10] ". . . the result of a change in genotypic constitution occurring independently of normal segregation, crossing over or irregular chromosome division; strictly, an alteration in the fundamental nature of the germ plasm, usually in a single gene." On the contrary, according to Brierley, most of the so-called mutations are really only the result of a recombination of the characters already

9. Brierley, W. B.: Variation in Fungi and Bacteria, Proc. Internat. Cong. Plant Sciences, Ithaca, 1926, vol. 2, 1929.

10. Jones, D. F.: Genetics in Plant and Animal Improvement, New York, John Wiley & Sons, 1925.

present. He believes that the occurrence of variations that revert to type supports his view.

It seems possible that the changes that occur in fungi could be the result of a loss or even of the rearrangement of factors when a character is determined by multiple factors. There is ample opportunity during one of the numerous vegetative mitoses for an unequal division of chromatin which would alter the character of that portion of the mycelium and of the spores subsequently formed on it.

Since Brierley's excellent treatment of the subject, a number of papers have appeared, and some of those dealing with fungi will be briefly reviewed. Chodat [11] described a mutant from Aspergillus ochraceus that regularly reverted to the parent type. He also obtained five races of Phoma alternariaceum. The mutants he studied varied in morphology and biologic activities. Dodge [12] has obtained an albino race of Neurospora sitophila which has given valuable data on the subject of hybridization in the fungi. Wiltshire [13] reported a strain of Alternaria that in single spore cultures repeatedly threw sectors bearing spores of the Stemphylium type. Mitter [14] described saltants of several species of Fusarium. He found that a given species might produce saltants that differed from each other more widely than many species of Fusarium. The saltants were usually less virulent in the production of apple rot than were the parent types. Mohendra [15] studied the effect of using different types of inocula in a number of fungi and found that subcultures from young mycelia, old mycelia and spores were identical. He obtained several saltants. Mohendra and Mitra [16] found that when spores from a single pycnidium of certain types of Sphaeropsis malorum are plated out they give four types of cultures. They rarely observed sectors, but believed that segregation of the bud variation type took place freely in the growing culture. Horn and Das Gupta [8] described a strain, DHB, of Diaporthe perniciosa from which a culture was obtained from one single hypha. This proved to be an "ever saltating" strain, DHC, which regularly after six days on standard mediums at room temperature reverted to the parent type, DHF. The "DHF zone"

11. Chodat, F.: Recherches expérimentales sur la mutation chez les champignons, Bull. Soc. bot. de Genève **18**:40, 1926.

12. Dodge, B. O.: Breeding Albinistic Strains of the Monilia Bread Mold. Mycologia **22**:9, 1930.

13. Wiltshire, S. P.: A Stemphylium Saltant of an Alternaria, Ann. Bot. **43**: 653, 1929.

14. Mitter, J. H.: Studies in the Genus Fusarium: VII. Saltation in the Section Discolor, Ann. Bot. **43**:379, 1929.

15. Mohendra, K. R.: A Study of the Changes Undergone by Certain Fungi in Artificial Culture, Ann. Bot. **42**:863, 1928.

16. Mohendra, K. R., and Mitra, M.: On the Cultural Behaviour of Sphaeropsis Malorum Pk., Ann. Bot. **44**:541, 1930.

progressed radially so that an old culture was entirely of the DHF type. DHF was stable, but on one occasion gave rise to a sector of the DHC type, thus giving a second example of reversion in the authors' studies. This report of an ever-saltating strain has already been mentioned in connection with the "pleomorphic" changes in the dermatophytes. Das Gupta [6] later reported further studies of Cytosporina, Phomopsis and Diaporthe, and described many saltants, some reversions and other ever-saltating strains. Many of the saltants suddenly appeared in a strain of Cytosporina that had for several years been stable but was then apparently "in a state of flux." This observation is also of interest for comparison with certain phenomena already described.

Leonian [17] made a study of variations in the genus Fusarium. In a later study [18] he attempted to induce myxochimera in a species of Fusarium by planting two strains together. He concluded that "a mere mixture of protoplasms cannot give rise to new characteristics unless there be a sexual phenomenon involved, because each nucleus will behave as a unit and develop its own characteristics."

Variations of another sort are reported by Barnes,[19] who induced variations by exposing spores of Eurotium herbariorum and of Botrytis cinerea to high temperatures. From some of the spores that survived this treatment he obtained forms that varied in pigmentation, sclerotial development and morphology. Ramchandani [20] described saltation in Bacillus violaceus and gave references to other literature on that subject.

The data on variation in the dermatophytes have not been described or interpreted in the light of the knowledge of mutations in other fungi, although variations have been frequently reported. One reason for this is that the most common variants do not occur as sectors. Spring [21] has described some of the variations that occur in hanging drop cultures. Biltris [22] observed variations within the species T. gypseum asteroides. Variants appeared as sectors in some cultures. He did not

17. Leonian, L. H.: Studies on the Variability and Dissociations in the Genus Fusarium, Phytopath. **19**:753, 1929.

18. Leonian, L. H.: Attempts to Induce "Mixochimaera" in Fusarium Moniliforme, Phytopath. **20**:895, 1930.

19. Barnes, B.: Variations in Eurotium Herbariorum (Wigg.) Link., Induced by the Action of High Temperatures, Ann. Bot. **42**:783, 1928. Variations in Botrytis cinerea Pers., Induced by the Action of High Temperatures, ibid. **44**:825, 1930.

20. Ramchandani, J. C.: Saltations in Bacteria: III. Bacillus violaceus, Ann. Bot. **44**:975, 1930.

21. Spring, D.: Morphologic Variation Within the Same Species of Dermatophytes as Observed in Hanging-Drop Cultures, Arch. Dermat. & Syph. **23**:1076 (June) 1931.

22. Biltris, R.: Sur la variabilité des caractères de l'espèce chez les dermatophytes, Ann. Inst. Pasteur **43**:281, 1929.

use single spores in obtaining his cultures. De Beurmann and Gougerot [23] described under the term "pleomorphism" changes sometimes appearing as sectors in species of Sporotrichum. Sabouraud [24] described different types of pleomorphism in Microsporum lanosum. Many other investigators have reported minor variations in growth.

There is no doubt that variations in the dermatophytes often occur. Because a colony shows no sectors of atypical growth it is not certain that there are no abnormal spores or hyphae in older parts of the colony. Indeed there is every reason to believe that the "pleomorphic" overgrowth arises from such modified spores or modified portions of the mycelium. The variants here studied, with one exception, manifested themselves in the old cultures within which they arose as small points or tufts or knobs of atypical growth. Transfers from these points to fresh mediums gave the variant opportunity to develop. Patient study of old cultures and of cultures on unusual substrates will undoubtedly yield many variants among these forms which seem to be unstable in morphology.

The appearance of these new forms in pure cultures with a known history is of interest to the mycologist and the dermatologist. Six distinct variants have arisen among the progeny of one microconidium. According to our present criteria for species lines, these might have been described as new species had they been isolated from lesions on different patients. Their appearance in pedigreed cultures in the laboratory shows that their status is only that of varieties or strains of the parent organism.

It is of great importance to the clinician as well as to the taxonomist to have data on the origin in pedigreed cultures of new types of dermatophytes. Fungus spores from different species vary in their response to fungicides. Different dermatophytes vary in virulence. The relative virulence of these variants is not yet known. It may be possible to show here, as it has been shown in other cases, that most of the variants are less virulent than the parent types. But it is equally possible that some are more virulent. If new varieties can arise in the culture flask, they can arise in nature. The variants of Achorion gypseum arose on a substrate that is in many respects like that on which the fungus grows on the human body. Their appearance under such circumstances leads one to believe that many of the dermatophytes now known as species are only varieties of a single unstable species.

23. de Beurmann, C. L., and Gougerot, H.: Les sporotrichoses, Paris, Félix Alcan, 1912.

24. Sabouraud, R.: Les teignes, Paris, Masson & Cie, 1910.

MULTIPLE BASAL CELL EPITHELIOMAS ORIGINATING FROM CONGENITAL PIGMENTED BASAL CELL NEVI

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No case similar to the one here reported could be found in the literature. The patient's history follows.

REPORT OF CASE

A healthy woman, aged 38, had had numerous pigmented moles scattered over her face and neck since she could remember. One on her neck grew to a size of 15 by 20 mm. in childhood but had since remained quiescent. Except for this, they caused her no trouble until ten years prior to the time of this report when a mole on the left side of her nose began to grow. After it had attained a moderate size the condition was diagnosed as "lupus" and was treated energetically with the roentgen rays. So much of the cartilage was destroyed, either by the process or by the treatment, that surgical removal was necessary, and a skin graft of full thickness was made to remedy the defect in the nose. There has been no recurrence of the lesion in the graft. About two years ago another mole on the right side of the nose commenced to enlarge; it attained a diameter of 15 mm. and involved the cartilage. A third mole beneath the right eye also began to grow at about the same time and reached a diameter of 8 mm. Most of the pigmented nevi have remained unchanged, but quite a number have enlarged slightly in the past two years, not, however, taking on the character of epitheliomas.

The description of the lesions falls naturally into that of the three types present. The original pigmented nevi, as yet unchanged, numbered fifty or more; they were scattered over the forehead, upper and lower eyelids and malar region, and a few were present elsewhere on the face and neck (fig. 1). They were dark brown, 1 mm. or less in diameter, flat, nonhairy lesions which were like the ordinary, small, brown pigmented nevi so frequently present on the face.

Microscopically (fig. 2) the lesion consisted of a wedge-shaped mass of cells, wide end up, apparently arising from the basal cell layer of the epidermis. The cells stained darker, but more nearly resembled the basal cells than any others. There were no cells suggestive of the nevus cell nests described by Gans.[1] In this mass of cells were a few scattered pigment (melanin)-bearing cells, which in a few places formed large collections. There were no mitoses, no apparent invasive properties and no inflammatory reaction in the surrounding tissue.

About twenty of these nevi, chiefly on the eyelids, recently began to enlarge and attained the size of a match head, being from 2 to 3 mm. in diameter (fig. 1).

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From Rush Medical College.

1. Gans, Oskar: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1928, vol. 2, p. 234.

They were elevated, translucent, umbilicated papules. In most of them the brown pigmentation of the original nevus was present in the dimple, but in some it was absent. The latter papules resembled the lesions of molluscum contagiosum more than anything else.

Microscopically (fig. 3) they resembled the original lesion. Cells that were like dark-staining basal cells originated from the epidermis and formed a large round mass, which was subdivided into several larger and smaller islands. In some places the origin from the basal cell layer of the epidermis could be seen. The center of the lesion, at the umbilication, had lost its epidermal covering. There were a few pigment-bearing cells scattered through this cell mass. The larger (15 by 20 mm.) elevated, pigmented lesion on the neck, which had enlarged in childhood and since remained quiescent, was essentially a larger edition of the molluscum-

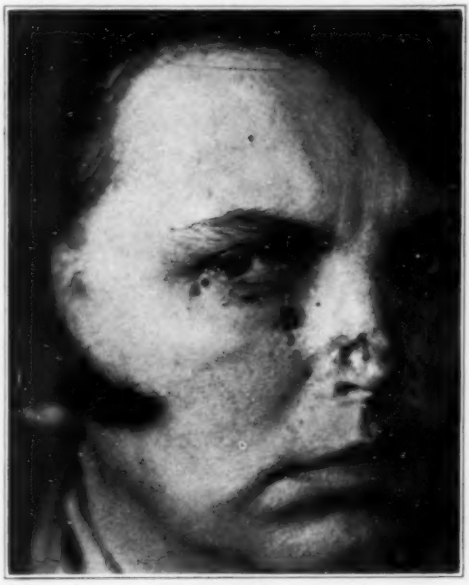

Fig. 1.—The original nevi are seen best on the forehead, the molluscum-sized ones at the outer angle of the eye and the epitheliomas on the nose and beneath the right eye.

like lesions. It consisted of numerous (fig. 4) islands of similar cells arising from the basal cell layer at the surface, and contained few pigment cells. There were no mitoses, no apparent invasive properties and no inflammatory reaction in the surrounding tissue.

Because of this lack of activity in all three lesions, the origin from the basal cell layer of the epidermis, the dominant basal cell type of cell, the presence of pigment cells and the essential similarity, they were considered as quiescent basal cell nevi.

Two frank epitheliomas, developed from the nevi, were present. One was 15 mm. in its largest dimension and was on the right side of the tip of the nose, where it had invaded the cartilage, but had not perforated it. On its border there were definite pearly nodules of small size with some crusting; the center had a

glazed appearance. There was little pigmentation in the lesion. The second epithelioma was 8 mm. in diameter and was located beneath the right eye. It was slightly crusted, was pigmented and had a typical threadlike border.

Microscopic examination of the latter lesion showed a rather invasive epithelioma arising from multiple foci from the basal cell layer of the epidermis. Most of the epithelioma cells were of the basal cell type, but there were several larger cells, and in one place only there was a suggestion of formation of a pearl. This observation might place the lesion in the class of basal squamous cell epithelioma, a condition the data on which were recently reviewed by Montgomery.[2] There

Fig. 2.—Section from an unchanged nevus, 1 mm. in diameter, on the forehead. There are several artefacts, but the origin from the epidermis can be seen. The cells are like dark-staining basal cells. A mass of pigment cells is in the center near the epidermis. Hematoxylin-eosin; reduced from a magnification of × 210.

was a rather dense infiltrate of round cells, plasma cells and other forms of cells in, between and around the invading epithelioma strands. There were only rare pigment cells in the infiltrating epithelioma cells.

The epitheliomas were intensively treated with the roentgen rays and electrodesiccation, while the nevi were removed by fulguration. None of the lesions showed activity after a year's observation.

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2. Montgomery, Hamilton: Basal Squamous Cell Epithelioma, Arch. Dermat. & Syph. **18**:50 (July) 1928.

Multiple epitheliomas arising in keratoses in persons who are much exposed to wind and sun, such as farmers and sailors, are fairly common. Multiple epitheliomas are usually present in xeroderma pigmentosum. Aside from these conditions, multiple epitheliomas of the face are rare. Multiple superficial epitheliomas, a condition recently studied by Wise,[3] rarely occur on the face, but Pautrier [4] reported an unusual case in which there were hundreds of superficial epitheliomas on the body and about twenty basal cell epitheliomas on the face.

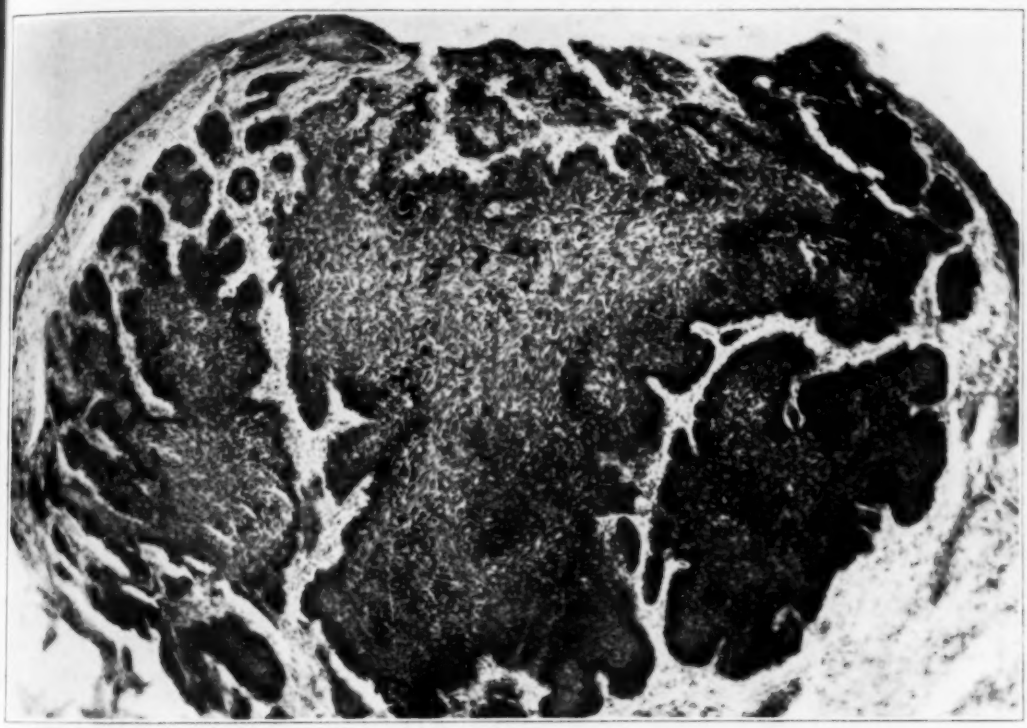

Fig. 3.—Section from a molluscum-like lesion on the right eyelid. The cell type is the same as that in figure 2. The origin from the epidermis can be seen at the edge of the "crater" on the left. There are a few pigment cells in the center of the large "island." Hematoxylin-eosin; reduced from a magnification of × 110.

3. Wise, Fred: Multiple Superficial Benign Epithelioma of the Skin: Its Differentiation from Kindred and Similar Eruptions, Arch. Dermat. & Syph. **19**:1 (Jan.) 1929.

4. Pautrier, L. M., and Archambault, G.: Cas extraordinaire d'épithéliomatose cutanée: plus de 200 foyers d'épithéliomatoma évoluant depuis 23 ans sur l'ensemble des téguments, sans retentissement sur l'état général et présentant, 5 types histologiques différents, Bull. Assoc. franç. p. l'étude du cancer **16**:835, 1927.

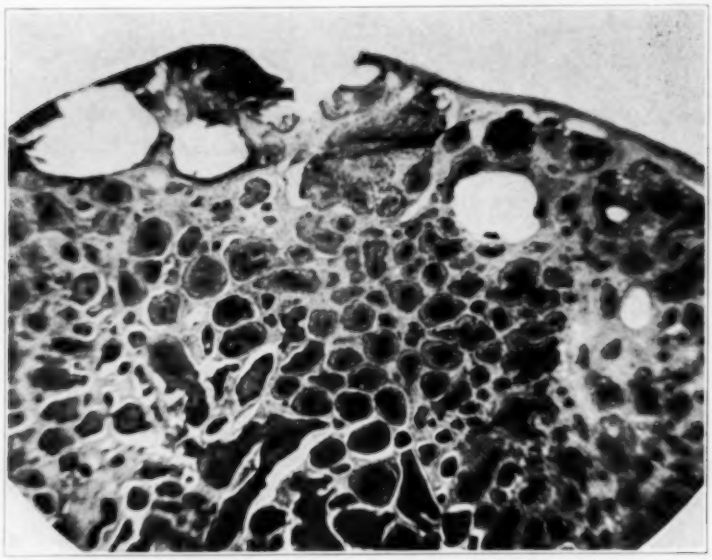

Fig. 4.—Section from a larger resting lesion on the neck. Hematoxylin-eosin; × 25.

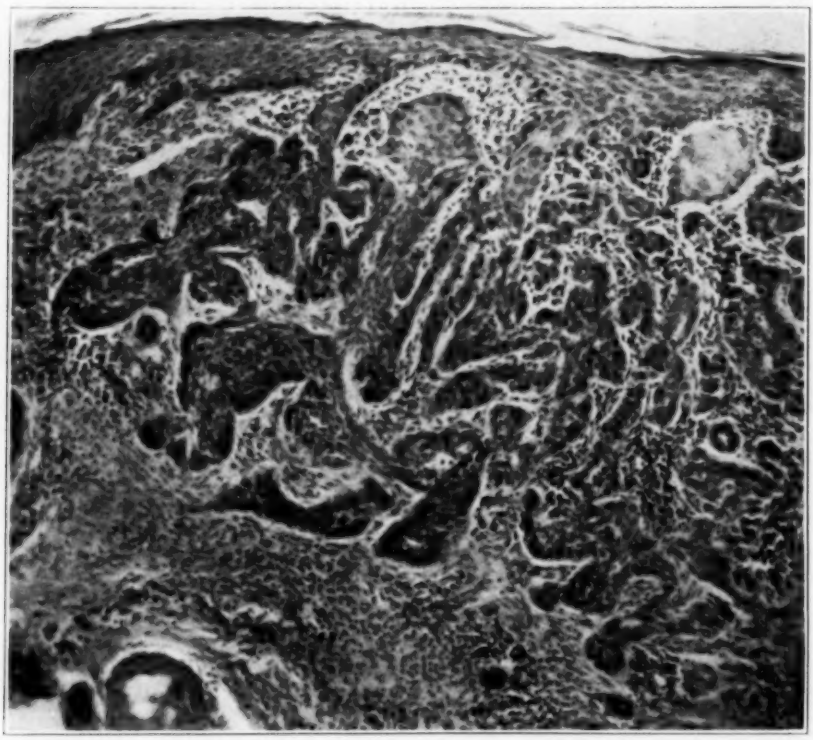

Fig. 5.—Section from an epithelioma beneath the right eye. Note multiple origin from the epidermis of a basal cell type of new growth. There is a suggestion of a pearl near the surface on the right. Note rather marked cellular infiltrate in and around epithelioma strands. Hematoxylin-eosin; × 110.

Adamson [5] described multiple basal cell epitheliomas of the face, not arising in keratoses, which, except for the lack of pigmentation and the fact that they did not arise from preexisting nevi, are similar to those in the case reported. There were numerous lesions, ranging from translucent, small, papule-like ones to typical ulcerating basal cell epitheliomas more than 25 mm. across. He considered them nevoid in origin, even though they did not arise from moles. He thought them a connecting link between ordinary rodent ulcer and epithelioma adenoides cysticum of Brooke.[6] White [7] and Stelwagon [8] described similar cases, but thought the condition should be considered as epithelioma adenoides cysticum. This I believe to be erroneous, as epithelioma adenoides cysticum is now generally considered to be a familial disorder in which the lesions do not undergo epitheliomatous degeneration. Little [9] presented similar cases in which he was uncertain whether the condition was multiple rodent ulcers or epithelioma adenoides cysticum. Adamson [9] considered these as cases of multiple rodent ulcer. Ormsby [10] presented a similar case.

Pigmented basal cell epithelioma, recently described by Bloch,[11] is rare. The lesions were on the body in his cases and did not arise in previously present pigmented nevi; they did not bear any resemblance to those in the case reported. The nevus that gives rise to malignant melanoma (Gans,[1] Kyrle [12]) is different histologically from those in the

5. Adamson, H. G.: Two Cases of Multiple Rodent Ulcer: With a Note on the Possible Relationships Between Rodent Ulcer and Epithelioma Adenoides Cysticum of Brooke, Lancet **2**:1133 (Oct. 17) 1908; On the Nature of Rodent Ulcer; Its Relationship to Epithelioma Adenoides Cysticum of Brooke and to Other Trichoepitheliomata of Benign Naevoid Character; Its Distinction from Malignant Carcinoma, Lancet **1**:810 (March 21) 1914.

6. Brooke, H. G.: Epithelioma Adenoides Cysticum, Brit. J. Dermat. **4**:269, 1892.

7. White, James C.: Multiple Benign Cystic Epithelioma, J. Cutan. & Genito-Urin. Dis. **12**:477, 1894.

8. Stelwagon, Henry W., and Gaskill, Henry Kennedy: Treatise on Diseases of the Skin, ed. 9, Philadelphia, W. B. Saunders Company, 1921, p. 681.

9. Little, E. G. Graham: A Note on Two Cases of Epithelioma Adenoides Cysticum (Brooke), Tricho-Epithelioma Papulosum Rodens (Jarisch), Brit. J. Dermat. **26**:173 (May) 1914. Adamson, in discussion on Little, E. G. Graham: Case: Multiple Rodent Ulcer (?) or Epithelioma Adenoides Cysticum, Proc. Roy. Soc. Med. (Sect. Dermat.) **8**:49 (Nov.) 1914.

10. Ormsby, Oliver S.: Case: Multiple Epitheliomas, Arch. Dermat. & Syph. **21**:667 (April) 1930.

11. Bloch, Bruno: Ueber benigne nicht naevoide Melanoepitheliome der Haut nebst Bemerkungen über das Wesen und die Genese der Dendritenzellen, Arch. f. Dermat. u. Syph. **153**:20, 1927.

12. Kyrle, Joseph: Vorlesungen über Histo-Biologie der menschlichen Haut und ihrer Erkrankungen, Berlin, Julius Springer, 1925, vol. 1, p. 95.

case reported, containing many nevus cells in "nests" and more pigment. In addition, these lesions are highly malignant, a condition obviously not true in the present case.

No cases identical with the one here reported were found in a fairly thorough search of the literature. The closest similarity found was in the cases reported by Adamson and in others of multiple basal cell epitheliomas of the face not arising in keratoses. The lesions described varied from small translucent papules to large rodent ulcers, but they did not arise in preexisting nevi as in the present case.

CONCLUSION

A case, apparently unique in the literature, is described in which epitheliomas arose in adult life from pigmented basal cell nevi present since birth.

TUBERCULOSIS CUTIS

AN UNUSUAL CASE

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We recently observed an unusual case of proved tuberculosis cutis that was very superficial in its clinical appearance and relatively benign in its course. Some textbooks in describing this type mention the existence of a flat or macular form of lupus vulgaris, but give no further description. In searching through the literature, we were unable to find any reference to a case of tuberculosis cutis that had remained superficial and had produced very little damage over a long period (eight years in our case). It is certainly not very frequently observed that lupus throughout its development retains its flat form and remains on the skin level.[1] In general, the human skin has a tendency to react with hypertrophy to a chronic toxin such as the tubercle bacillus.

Volk [2] stated that in the early stages of the lupus nodule, the surface is practically unchanged, and that under certain circumstances, the infiltration remains on the same level as the surrounding normal skin. In our case, the character of the lesions may possibly be explained by some of the findings to be described.

REPORT OF A CASE

History.—I. D., a man, aged 35, born in Russia, was admitted to the otological service of Dr. S. J. Kopetzky at the Beth Israel Hospital on Feb. 3, 1931. The patient's mother had died of cancer at the age of 62. The father was living and well. The patient had measles and chickenpox during childhood. Twenty-four years before this examination he had had a mastoidectomy performed on the left side. For the past twelve years he had suffered from pulmonary tuberculosis. About ten years ago, he was operated on for "intestinal trouble," probably tuberculosis, according to the patient. Venereal infection was denied by name and

Submitted for publication, Aug. 17, 1931.

1. Volk, R.: Tuberculose der Haut, in Jadassohn, J.: Handbuch der Haut und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 10, pt. 1, p. 222.
2. Volk (footnote 1, p. 220).

symptom. He had been married for eleven years and had two children who were living and well. His wife had never had a miscarriage.

About a year before the present examination, the left mastoid that had previously been operated on began to discharge greenish-white pus. About eight years ago, the patient noticed a small reddish patch on the skin over the right hip. This enlarged very slowly, and, at varying intervals up to about four months ago, new patches made their appearance.

Examination.—The patient was a fairly well developed man. There were many hard, round, well defined glands, the size of marbles, in the left and right postcervical chains. There was a discharging sinus on the left mastoid process. Examination of the chest revealed old chronic pulmonary tuberculosis with moderately extensive lesions involving both upper lobes (right and left).

There were disseminated patches of a generalized eruption. The patches varied in size from that of a nickel to that of an adult palm. The color varied from the bright red of subacute inflammation to that of chronic psoriasis, and yet it was not as violaceous as in lichen planus. With this redness there was also a faint

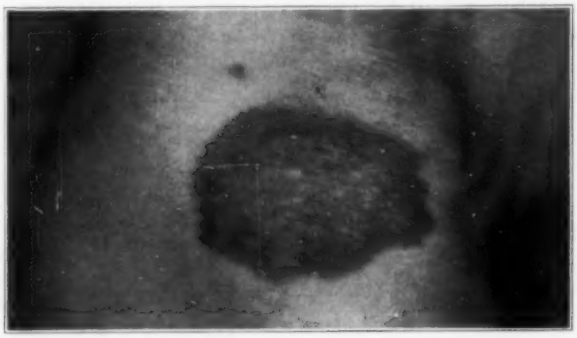

Fig. 1.—This lesion is the oldest (eight years). Its resemblance to other dermatoses is quite evident.

but distinct yellow tint. The patches were irregular in outline, and the smaller lesions faded imperceptibly into the surrounding normal skin, as in eczema. The older lesions showed a more distinct edge. The surface of the lesions was flat, not elevated, covered with fine adherent scales, gray and yellow-gray, and in places there seemed to be a slight thinning and atrophy in the central area of the lesions. Scattered over these macular lesions were pinpoint to pinhead-sized, circumscribed areas, which were revealed by close examination only, and which, on pressure, occasionally showed the crumbling and bleeding seen in lesions of lupus vulgaris. In no place was there any discernible infiltration on palpation. There was no necrosis, softening or ulceration present, nor were there any shiny scales or bleeding points on removal of the scales, as in psoriasis. No outlying tubercles were to be found. In the areas in which biopsies were performed, the resulting scars were elevated, keloidal, somewhat puckered and of typical "apple jelly" color.

Otologic Findings.—The patient was operated on by Dr. Ralph Almour. An abstract of his report follows:

At operation, there was a great deal of new bone formation present in the old operative cavity. In the region of the antrum, there was a large cavity which was filled with exuberant and unhealthy granulations, and which had exposed the

dura of the middle cranial fossa. The rest of the bony wall of this cavity was necrotic and crumbled easily on being touched. The granulations found were yellow and very suggestive of a tuberculous involvement. Five days later, a plastic operation was performed. After primary union of the wound and good healing for a period of three weeks, there gradually began to appear several spontaneous fistulous openings through which a thin, watery discharge exuded. This clinical picture is characteristic of a tuberculous lesion of the mastoid process and of the middle ear.

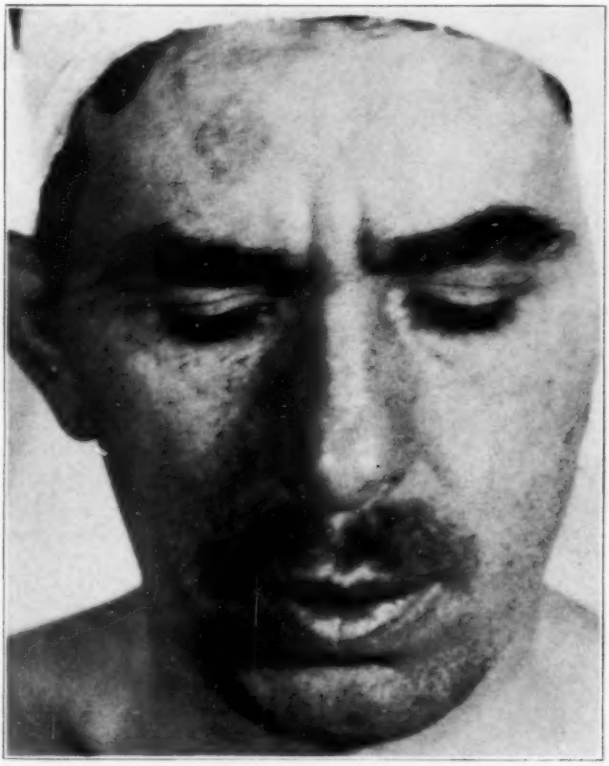

Fig. 2.—Note the superficial character of the patch on the right side of the forehead.

Histologic Examination.—The section used for examination was a piece of skin excised from one of the older lesions on the abdomen.

Low power magnification showed the epidermis to be partly thinned and the rete pegs somewhat flattened. The cutis showed diffuse infiltration in its upper part.

High power showed that immediately beneath the epithelium the corium was diffusely infiltrated with granulation tissue containing fibroblasts, small round cells and histiocytes. There was some separation of the connective tissue bundles. In several areas of the corium there were concentrations of the cellular element. In these, the fibroblastic cells showed a more or less sweeping circular arrangement.

on the periphery of which were a number of rather large, multinucleated Langhans cells. There were irregular strands of this same granulation tissue extending into the deeper subcutaneous connective tissue reaching the level of the sweat glands. One hair follicle was surrounded by this cellular granulation tissue, with one or two rather indistinct giant cells in the periphery. In the deeper portion, the connective tissue bundles were wider, showed focal hyalinization and a distinct absence of the cellular infiltrate. Surrounding the duct of one of the sweat glands were a small amount of granulation tissue and some giant cells. Blood vessels were unusually sparse and were of the precapillary arteriole type. The lymph channels were best seen in the subepithelial corium and were slightly dilated.

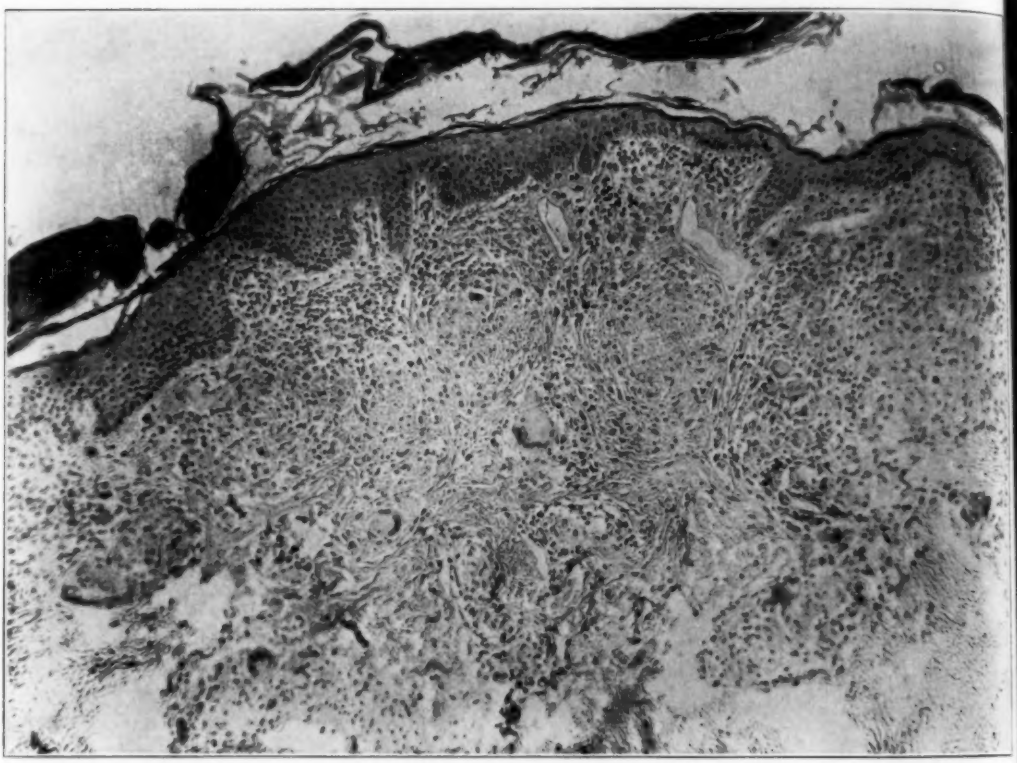

Fig. 3.—Note the presence of the infiltration mainly in the upper part of the corium. Low power photomicrograph.

In general, the infiltration was noteworthy because of its presence mainly in the subepithelial corium and its invasion of the papillae. This may explain, in part, the superficial character of the lesions.

Laboratory Data.—The Wassermann reaction of the blood was negative. Repeated urinalyses and a blood count revealed no abnormalities. Roentgen examination of the chest showed an acinous exudative phthisis of both upper lobes associated with productive changes. The Pirquet tuberculin reaction was negative, but the Mantoux reaction was positive. Examinations of the sputum demonstrated the presence of tubercle bacilli.

On March 3, 1931, a guinea-pig was inoculated with an emulsion of tissue obtained from one of the younger skin lesions. After three months, during which the animal appeared to be in good health, it was killed, and an autopsy performed. All the organs and the peritoneal cavity were apparently normal. On the parietal peritoneum and the adjacent abdominal wall, apparently along the route of injection, there was a pea-sized collection of greenish pus. Examination of this pus by the bacteriologist revealed the presence of tubercle bacilli. This localized infection in the guinea-pig certainly points to a low grade virulence of the tubercle bacilli.

COMMENT

In studying this case, we were impressed by the clinical resemblance to the diffuse infiltrating type of Boeck's sarcoid. Lewandowsky,[3] in describing this form of sarcoid, stated that the lesions in the beginning are red, and later become violaceous. He also stated that there is some infiltration of the cutis, and that the lesions are not sharply demarcated from the healthy tissue. In addition, he noted that pressure with a glass slide reveals small lupus-like nodules of a yellowish tinge, that these nodules coalesce to form the diffuse type of lesion, and though this is usually associated with the nodular form of Boeck's sarcoid, it may occur alone.

It is quite evident that the clinical descriptions of the lesions of our case and of the foregoing condition bear a great deal of resemblance to each other. The pathologic picture in this type of sarcoid usually shows an infiltration of the cutis and not of the subcutis. Well developed giant cells, as well as lymphocytes, plasma cells and mast cells, are scarce in most of these cases. There is a constant close relationship between the infiltrate and the blood vessels. Though the histologic observations just mentioned are usually associated with sarcoid, Volk [4] emphatically denied the specificity of this picture for sarcoid. He believed that tuberculids and true tuberculosis, like lupus, can present a similar histologic appearance. The recovery of tubercle bacilli by guinea-pig inoculation does not eliminate the diagnosis of sarcoid, because Kyrle,[5] Boeck [6] and also Ruete [7] demonstrated the presence of these organisms in cases of sarcoid.

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3. Lewandowsky, F.: Die Tuberculose der Haut, Berlin, Julius Springer, 1916, p. 201.

4. Volk (footnote 1).

5. Kyrle, J.: Die Anfangstadien des Boeckschen Lupoids; Beitrag zur Frage der tuberkulösen Aetiologie dieser Dermatose, Arch. f. Dermat. u. Syph. **131**:33, 1921.

6. Boeck, C.: Nochmals zur Klinik und zur Stellung des benignen Miliarlupoids, Arch. f. Dermat. u. Syph. **121**:707, 1916.

7. Ruete, A.: Zur Aetiologie der Bocckschen Erkrankung, Dermat. Ztschr. **37**:129, 1922.

Schaumann [8] observed an erythematous form of Boeck's sarcoid that varied from a pale red to a violaceous color, and that occurred mainly on the lower extremities. The eruption showed hardly any infiltration. Histologically, there were infiltrations around the blood vessels and the skin appendages. He called the lesions "forme erythrodermique" of Boeck's sarcoid.

Sweitzer [9] described a case of tuberculid en plaque that resembled our case only in its early macular lesions and only slightly in its histologic appearance. Our case did not present the hard and raised plaques he described in his patient.

Consideration of the diagnosis in our case also involved ruling out psoriasis, parapsoriasis, eczema, lupus erythematosus, premycosis fungoides, leukemia cutis and syphilis. The predilection for the extensor surfaces, the micaceous scales and the bleeding points seen in psoriasis were absent. The superficial persistent lesions with their thin adherent scales suggested parapsoriasis. The presence of the "apple jelly" colored areas, together with the slight atrophy, served, however, to distinguish the case from this condition. There were no crusting, oozing, vesiculation and itching or the indefinite course seen so frequently in eczema. Lupus erythematosus was not easily excluded. The indolent course, the slight scaling and atrophy and the absence of nodules and ulceration did suggest this condition. However, the lack of gaping follicles with sebaceous plugs and the presence of the "apple jelly" colored areas served to point more to tuberculosis cutis. Premycosis fungoides was considered, but there was no itching, and the course of the lesions did not show the capriciousness of this condition. Leukemia cutis was ruled out by the presence of a normal blood count. The nonulcerating syphilid could not be considered because of the absence of infiltration, induration and other stigmas of syphilis and the presence of a negative Wassermann reaction. The dermatoses enumerated were mentioned to illustrate some of the difficulties of a clinical diagnosis in our case. On the other hand, these conditions were easily excluded by the microscopic picture, which was that of frank tuberculosis cutis.

It was obviously difficult to place our case with any degree of certainty either in the category of true tuberculosis or of sarcoid. We felt, however, that as the skin condition showed all the evidences of tuberculosis and was associated with tuberculosis of the lungs and mastoid, it was correct to classify the lesions as tuberculosis cutis.

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8. Schaumann, in Volk (footnote 1, p. 388).

9. Sweitzer, S.: A Case for Diagnosis, Arch. Dermat. & Syph. **15**:354 (March) 1927.

SUMMARY AND CONCLUSIONS

1. A report is made of an unusual case of tuberculosis cutis occurring in a person with tuberculosis of the lungs and of the left mastoid bone.

2. The cutaneous lesions were very superficial and relatively benign in their course.

3. The diagnosis was made partly on the basis of the clinical appearance of the lesions and positively by the histologic examination and the recovery of the tubercle bacilli after inoculation of a guinea-pig.

4. Difficulty was encountered in differentiating this condition from other cutaneous diseases, particularly from Boeck's sarcoid.

5. It is our belief that the pathogenesis of these lesions is dependent on an attenuated form of the tubercle bacillus.

EFFECT OF POSITION OF INOCULUM ON GROWTH OF SOME TRICHOPHYTONS IN THE PRESENCE OF DYES

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The influence of biologic dyes on bacteria and fungi is too well known to be reviewed here; this also applies to the comparative efficiency of different stains. But so far as I am aware, no work has been done on the effect of the position of inoculum in the presence of toxic substances. This is perhaps due to the fact that cultural methods have been so well standardized that few investigators feel the necessity of developing a new or different technic. The bacteria that stick to the transfer needle or any hyphae that can be jerked away from a test tube culture and transferred to a fresh medium constitute the inoculum. No two pieces of inoculum are alike either in quality or in quantity; nor have any of them the same position after they have been transferred. But the investigator does not worry about this, nor does he feel the necessity for concern.

I have developed a technic whereby the quality, the quantity and the position of the fungal inoculum can be easily standardized, and I have used this method for several years. Petri dish cultures are substituted for test tubes, each dish containing 20 cc. of the nutrient agar; the colony is allowed to grow until it assumes a suitable size. A cork borer with an opening 5 mm. wide is then used to cut inoculum disks all along the margin of the colony. These inoculum disks, all having the same size and age, can then be lifted by a hooked platinum needle and transferred in any position to any given substratum. If the inoculum is transferred upside down, so that the mycelial surface comes in contact with the substratum while the agar part is away from it, there may ensue no growth and the inoculum may die, whereas the reverse position of the inoculum may cause good growth and induce no apparent ill effect. This is strikingly demonstrated in the following table, which shows the results obtained when about twenty-six trichophytons were subjected to the action of various concentrations of malachite green and crystal violet. These organisms were secured from Centraalbureau, Holland, the American Type Culture Collection and Dr. Fred D. Weidman.

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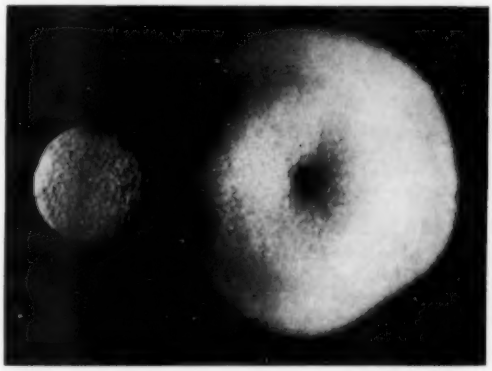
The medium used for the growing of trichophytons is one I developed in connection with some other studies; it consists of the following ingredients: proteose peptone, 5 Gm.; bactodextrose, 20 Gm.; dihydrogen potassium phosphate, 1 Gm.; magnesium sulphate, 1 Gm.; agar-agar, 20 Gm., and water, 1,000 cc. This medium supports a fine growth, induces good colony differentiations and gives excellent color reactions with the chromogens. For the present studies the agar-agar content was reduced to 0.4 per cent, just enough to form a soft gelatinous mass and thus prevent the inoculum disks from sinking. Enough of the dye was added to yield concentrations of 1 part of the dye in 50,000 and 100,000 parts of the medium. Five cubic centimeters of the medium was then poured into each test tube and sterilized at 10 pounds



T. gypseum lacticolor on nutrient agar containing malachite green (1:25,000). Left, thin inoculum disk, cut from petri dish culture containing only 15 cc. of nutrient agar; right, thick inoculum disk, cut from petri dish containing 30 cc. of nutrient agar. Both inoculum disks were transferred on the same day and with the agar side next to malachite green agar. The thin inoculum disk failed to grow even after six weeks, while the thick inoculum disk made a fairly good growth. The thickness of the agar enabled the fungus to emerge from the lag period before enough of the dye was diffused through the disk to reach the fungus and inactivate it, whereas the thinner disk failed to serve as an efficient barrier.

(4.5 Kg.) of pressure for fifteen minutes. The tubes were not slanted, but were allowed to harden in an upright position. Transfers were then made; in one series all inoculum disks were transferred with the mycelium side next to the agar, and in the other series away from the agar. Two weeks later readings were made. Readings made one month later showed no marked difference in the results. Consequently a two weeks' period is considered sufficient, with few exceptions, to give a representative idea concerning the behavior of these organisms.

The relative growth of the different organisms is expressed by Roman numerals: O means no growth; V, an abundant growth, and the intermediate numerals, intermediate results. For lack of a better method of expression, Roman numerals will serve the purpose. After all, the important thing is not the relative growth, but the presence or absence of growth.

The Effect of Position of the Inoculum on Growth of Some Trichophytons in the Presence of Dyes

	Malachite Green				Crystal Violet			
	1:50,000		1:100,000		1:50,000		1:100,000	
Organisms	Hyphae Up	Hyphae Down	Hyphae Up	Hyphae Down	Hyphae Up	Hyphae Down	Hyphae Up	Hyphae Down
T. asteroides gypseum Sabouraud	I,0	0,0	II,II	0,I	IV,III	IV,II	V,IV	V,III
T. crateriforme Sabouraud	I,0	0,0	II	0	V,V	V,V	V,V	V,V
T. declavans Castellani	0,0	0,0	0,0	0,0	III,IV	II,IV	III,IV	0,IV
T. discoides faviforme Sabouraud	0,0	0,0	0,0	0,0	II,III	0,I,III	II,III	0,III
T. equinum (Matruchot and Dassonville) Gedoelst	0,0	0,0	0,0	0,0	III,III	I,II	III,III	I,0,II
T. eryotrephon Papegaay	0,0	0,0	I,II	0,0	I,I	0,0	III,III	0,II,II,0
T. faviforme album Sabouraud	0,I,0	0,0	II,II	I,0	III,IV	II,III	III,IV	II,III
T. fumatum Sabouraud	0,0	0,0	I,I	0,I	V,V	V,V	V,V	V,V
T. granulosum Sabouraud	II,I	0,0	II,II	0,I	V	V	V	II
T. gypseum Horta	III,I	0,0	V,IV	0,III	V,III	V,II	V,V	V,IV
T. gypseum var. 1, Ballagi	II,I	I,0,0	IV,III	III,III	IV,II	III,0	IV,IV	III,IV
T. gypseum lacticolor Sabouraud	0,0	0,0	I,0	0	II,II	I,II	IV,III	II,III
T. interdigitale Priestley, no. 1	0,0	0,0	0,0	0,0	IV,III	III,II	V,IV	V,III
T. interdigitale no. 2	0,0	0,0	I,0	0,0	II,IV	II,III	III,V	II,V
T. lacticolor Sabouraud	I,II,0	0,0	0,V,III,0	0,0	V,IV	V,III	V,V	V,V
T. louisianicum Castellani	IV,III	0,0	V,III	0,II	III,I	0,I,0	IV,IV	0,0
T. megalosporum equinum	II,II,0	I,0,0,0	III,III	II,III	III,V	III,III	III,IV	III,II
T. nodoformans Castellani	I,0	0,0	IV,III	0,I	IV,II	0,0	IV,IV	II,IV
T. niveum Sabouraud	0,0	0,0	V,III	0,0	III,II,IV	0,0	V,IV	0,IV
T. niveum radians Sabouraud	0,0	0,0	IV,I	0,0	IV,V	II,V	V,V	V,V
T. ochropyrraceum Papegaay	0,0	0,0	0,II	0,I	0,V	0,V	I,V	I,V
T. purpureum Bang	0,I	0,0	I,I	0,0,I	III,III	II,0,III	III,IV	II,III
T. persicolor Sabouraud	0,0	0,0	V,IV	0,II	I,IV	0,I	II,IV	I,IV
T. radiolatum Sabouraud	0,0	0,0	0,II	0,I	II,III	I,II	II,III	I,III
T. rosaceum Sabouraud	0,I,0	0,0,0	II,III	0,0	III,II	III,II	IV,IV	IV,III
T. sulfureum T. Fox	0,0	0,0	I,0	0,0	III,0	III,II	III,V	III,V

The experiments were repeated four times, triplicate cultures being used in each. The results listed in the accompanying table merely show the representative average of all readings.

The first thing to be noted in the accompanying table is the decidedly inferior potency of crystal violet in restricting the growth of these organisms. This is true not only for trichophytons but for many other fungi with which I have worked for a number of years. But because

crystal violet gives such excellent results with bacteria, it is used much more frequently than malachite green, which seems to be generally less specific for bacteria than it is for fungi.

Many of the reactions here listed are decidedly erratic, despite a rigid uniformity of all conditions. T. lacticolor, for instance, may sometimes grow very well in the presence of 1 part of malachite green in 100,000 parts of nutrient agar; but when this experiment is repeated under identical conditions, the organism may show no sign of growth, and often the inoculum dies. Such conditions have been observed even in duplicate and triplicate cultures. Two pieces of inoculum, removed from the same colony and from the same region of the colony, seem to be in different physiologic conditions. I [1] have observed hundreds of such cases in other fungi and have followed them for a number of generations without finding constancy of behavior. In view of such inconstancy, it is doubtful whether the use of biologic dyes in such cases can be considered of much value in the work of identification.

The most noteworthy fact brought out in the accompanying table is the effect of the position of the inoculum on the growth of fungi in the presence of malachite green. It can be seen that whenever the concentration of the dye is critical enough for any of the organisms listed, growth generally occurs if the hyphal surface of the inoculum is away from the agar and suppression or death if the mycelial side of the inoculum is in direct contact with the medium. In this connection, it should be stated that often growth was induced even by such a change of position as the raising of one edge of the inoculum, so that only a part of it came in contact with the agar and the other part did not touch it. The underlying cause of this strange behavior is simple: when the inoculum was so placed as to bring the hyphae in direct contact with the agar and its content of dyes, the fungus was given no opportunity to adjust itself to the toxic substance and was thus inhibited or killed. But when the position was reversed, a layer of agar, which is an inseparable constituent of each inoculum disk, served to separate the mycelium from the dye. A comparatively slow diffusion of the dye from the medium into this layer of agar and thence to the hyphae was not sufficient to inhibit the fungus. The lag period constitutes the critical stage in the life, not only of bacteria, but of fungi as well. Environmental extremes that ordinarily are unable to cause much harm may, during this period, become controlling factors. The layer of agar of each inoculum disk serves as a sort of shock absorber and affords to the hyphae the opportunity to emerge successfully from the lag period and to launch into the actively growing phase. This, rather than possible acquired resistence, is to be considered the factor that

1. Leonian, Leon H.: Studies on the Variability and Dissociations in the Genus Fusarium, Phytopath. **19**:753, 1929; plates xvi-xxxiii.

enables a given organism to grow when the inoculum disk is transferred with its agar surface next to the dye and to be inhibited or killed when the hyphal surface is brought into direct contact with the dye. It should be understood, however, that this rule works within certain limits. If the concentration of the dye is too high, or if the dye is too potent even in dilute concentrations, the diffusion is sufficient to reach the fungus and kill it even after it has emerged from the lag period. On the other hand, if the concentration of the dye is not high enough, or if the dye is not sufficiently potent, growth will ensue despite the position of the inoculum.

Those who are working with differential growth may find it profitable to consider the position, the age and the quantity of their inoculums before they make generalizations.

Mr. W. D. Henry assisted in the laboratory procedure.

XANTHOMA TUBEROSUM

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In their paper on xanthoma tuberosum,[1] Weidman and Freeman stated that they considered this disease uncommon. They also said that they had added another case of involvement of the tendons to the list.[2] In the presentation of their cases, emphasis is placed on an unusual instance of xanthoma tuberosum with extensive tendon involvement, and a few less interesting cases of this disease are mentioned.

The differences of opinion regarding certain phases of this disease necessitate reports of new cases. Some writers are doubtful about classifying this condition under the group of neoplastic diseases and hesitate to consider the planum and tuberosum types of xanthoma as the same disease.[2] Stengel [3] considers the histology of xanthoma as that of modified fatty tissue resembling embryonal adipose tissue and its round cell infiltration as a tendency to sarcomatous change. However, he considers it a definitely benign disease. Krogius [4] reported a number of cases of xanthosarcomatous tumors of the tendon sheaths which appear to be benign at first, and which, if not removed surgically, become sarcomatous. The resemblance of the histopathology of this disease to sarcoma and the presence of an associated cholesteremia render it interesting from the point of view of recent reports connecting cancer of the skin with cholesteremia and richness of precancerous tissue in cholesterol.[5]

The etiology of the disease has certainly not been cleared up. Schamberg [6] considered age, jaundice and cholesteremia as possible factors. Senear [7] presented a case of xanthoma tuberosum multiplex occurring in a woman with latent syphilis. Xanthoma and diabetes have

Submitted for publication, Aug. 3, 1931.

1. Weidman, F., and Freeman, W.: Xanthoma Tuberosum, Arch. Dermat. & Syph. **9**:149 (Feb.) 1924.

2. Weidman and Freeman (footnote 1, p. 174).

3. Stengel, A.: A Text Book of Pathology, ed. 3, Philadelphia, W. B. Saunders Company, 1901, p. 233.

4. Krogius, A.: Xanthosarcomas of the Tendon Sheaths, Finska läk.-sällsk. handl. **64**:102, 1922.

5. Roffo, A. H.: Cholesterol in Cancer, Paris méd. **1**:282 (March 21) 1931; abstr., J. A. M. A. **97**:65 (July 4) 1931.

6. Schamberg, J. F.: A Compend of Diseases of the Skin, ed. 7, Philadelphia, P. Blakiston's Son & Co., 1925, p. 227.

7. Senear, F. E.: Xanthoma Tuberosum Multiplex Occurring in a Woman with Latent Syphilis, M. Clin. North America **10**:21 (July) 1927.

been intimately related. In some cases the hereditary character of xanthoma tuberosum is unquestionable. The connective tissue formation, the breaking down of lipoids and the deposits of cholesterol form the essential items of the pathologic picture of arteriosclerosis.[8] The degeneration of smooth muscle cells that is found in xanthoma [9] is also described in arteriosclerosis.[8] The association of diabetes, syphilis, an inherited predisposition and a nodular form of lesion,[8] with arteriosclerosis, have also been found in xanthoma.[10] In dealing with xanthoma, one must therefore seriously consider a number of diseases the outstanding characteristics of which are also found in this condition.

REPORT OF CASES

CASE 1.—An electrical engineer, aged 34, married, presented himself, on Aug. 27, 1929, giving a history of an injury to the big toe of the right foot. Roentgen examination revealed a fracture. In the course of manipulation of that extremity, a mass was noticed at the base of the toe, and on further examination and inquiry similar findings were made in symmetrical parts of the extremities. These masses were located in the tendons; they were most marked in the tendo achillis, that of the triceps muscles, those at the metacarpophalangeal junctions and the metatarsophalangeal region, and some took the form of a string of beads that could be felt deep in the palmar and plantar regions as they were distributed in the proximal and distal parts of the interosseus muscles. The patient claimed that this was the character of the full grown lesions in other parts of the body, seven years prior to examination. He related them etiologically to the excision of a cyst in the posterior aspect of the right elbow joint, because they were noticed a month subsequent to the operation. The lesions were of firm consistence except in the tendo achillis region, where they had softened, probably as a result of pressure and friction, and where they caused much discomfort.

There was no history of venereal or tuberculous infections. A brother, aged 51, presented similar lesions of four years' duration in the same regions; there was no history of trauma preceding the onset of the lesions. His two sons, aged 18 and 20, had similar lesions in identical locations, but in a milder form. The wife and children of the patient did not have this condition. There were no systemic disturbances other than those of the muscular system.

Examination.—Physical examination of the parts other than the skin and tendon regions gave normal results. Fluoroscopic and roentgen examinations repeatedly gave negative results. The patient was under observation for more than one and a half years, during which slight enlargement of the growths in the tendo achillis was the only change noted.

In figure 1, an attempt is made to present a composite picture of the major loci of involvement. In this figure, a prominence situated on the internal aspect of the upper portion of the left leg should be noted. It is in this locality, i. e., in the

8. Delafield, F., and Prudden, F. M.: A Text Book of Pathology, ed. 11, New York, William Wood & Company, 1919, p. 644.

9. MacCallum, W. G.: A Text Book of Pathology, ed. 2, Philadelphia, W. B. Saunders Company, 1920, p. 948.

10. MacCallum (footnote 9). Senear (footnote 7). French, H.: Index of Differential Diagnosis, ed. 4, New York, William Wood & Company, 1928, p. 405.

Fig. 1.—A composite picture of the major loci of involvement. Note the prominence on the internal aspect of the upper portion of the left leg.

Fig. 2.—*A*, the posterior and lateral aspects of the thickened tendo achillis. In *B*, the thickened tendons of the peroneus longus and brevis and a growth above the flexor hallucis longus tendon are shown.

Fig. 3.—The location of the masses in the hand. Compare these hands with the normal hands to the right.

region of the insertion of the composite tendons of the sartorius, gracilis, semitendinosus and semimembranosus that the growths assume the consistency of bone. A similar tendency to calcification is also found in the upper portion but anterior aspect of the right leg, where the patellar tendon is inserted. Figure 2 *A* shows the posterior and lateral aspects of the thickened tendo achillis. In figure 2 *B*, the thickened tendons of the peroneus longus and brevis and a growth above the

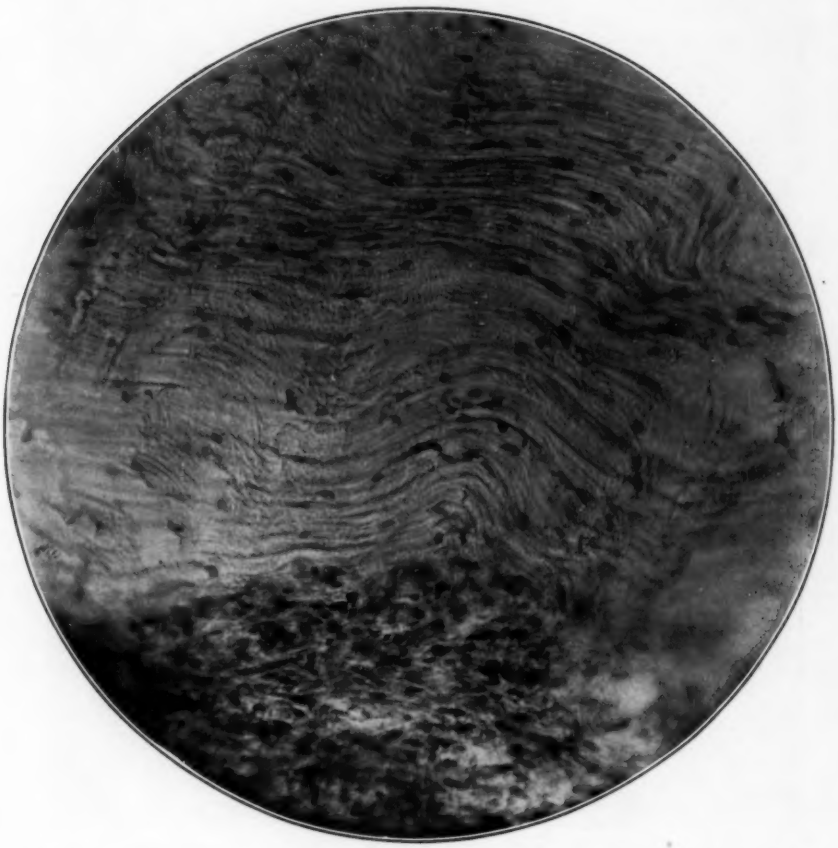

Fig. 4.—Photomicrograph showing the fibroblastic character and cellular reaction.

flexor halucis longus tendon are noticeable. In figure 3, the location of the masses in the patient's hand may be compared with those in the normal hand.

The planum variety of lesions were found in the palpebral regions.

Biopsy.—Biopsy revealed a smooth, glistening, yellowish tumor which grated on section. An alcoholic extract contained much cholesterol. The fibroblastic character of the tumor and the cellular reaction are presented in figure 4, while the typical xanthoma cells, lipoidal material and the peculiar stroma are shown in figure 5. In figure 6, cellular characteristics that give the impression of a malignant tumor are shown.

Laboratory Report.—An examination of the blood showed 112 per cent of hemoglobin, 6,250,000 erythrocytes and 4,900 leukocytes per cubic millimeter; the differential count revealed: neutrophils, 61 per cent; lymphocytes, 126 per cent; large mononuclears, 8 per cent; basophils and transitionals, 2 per cent each, and myelocytes, 3 per cent. Chemical examination of the blood gave these results:

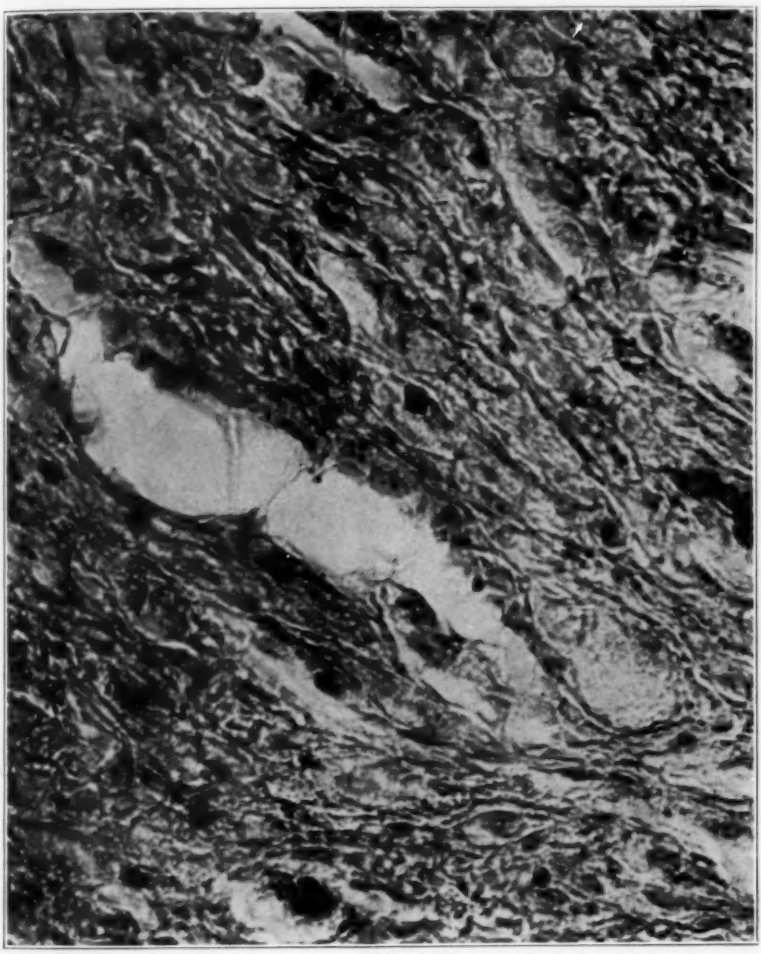

Fig. 5.—Photomicrograph showing the typical xanthoma cells, lipoidal material and the peculiar stroma.

nonprotein nitrogen, 34.3 mg.; cholesterol, 300 mg., and blood sugar, 148 mg. per hundred cubic centimeters; these substances were found in greater amounts per cubic centimeter in the blood of the patient than in the normal person. The Wassermann reaction of the blood was negative. The coagulation and bleeding times were five and fourteen minutes, respectively, and the clot retraction was forty minutes.

Case 2.—G. M., a woman, aged 55, who came to my attention in December, 1929, gave a history of headache, indefinite and general pains of a neuralgic character, chronic constipation and insomnia. The family and past history revealed nothing of significance.

Physical examination gave normal results, except for masses under the skin which were not distributed along the nerves; they varied in size from that of a pea to that of a cherry, and were of the same consistency as those noted in the first patient. Urinalysis gave negative results.

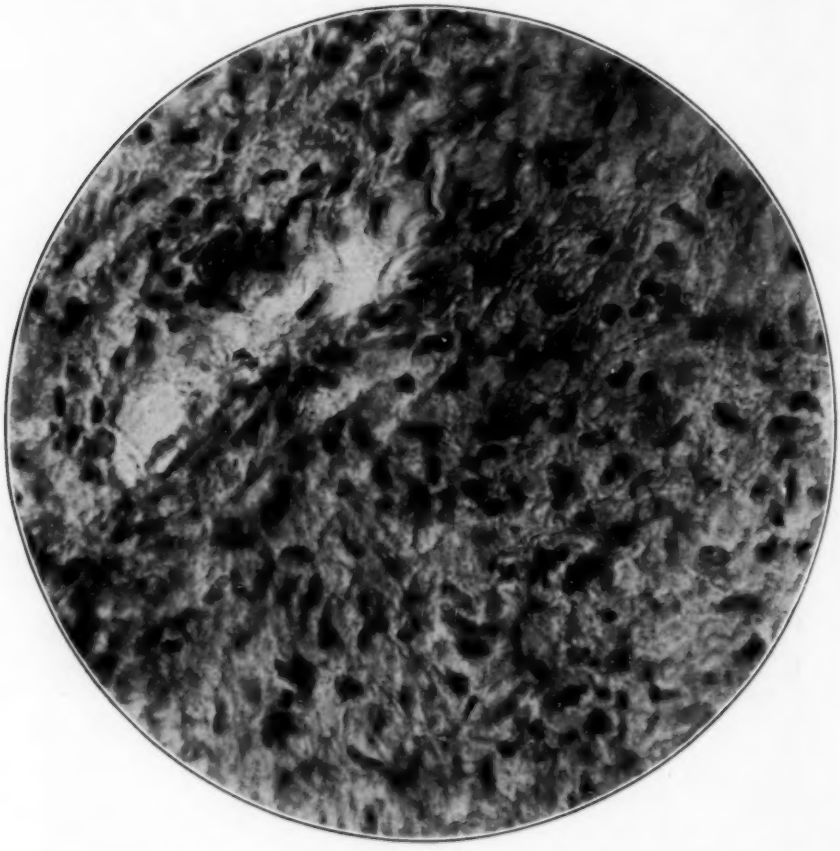

Fig. 6.—Section of the tumor showing a tendency to sarcomatous cellular changes.

Case 3.—*History.*—A third patient suffering from this disease showed masses like those of the second patient in size, consistence and distribution when he first came to my office in February, 1930. He was 66 years of age, and presented a history of diabetes of six years' duration and of an attack of acute nephritis a year prior to the probable onset of the diabetes. He complained of a sensation of heaviness in the epigastric region, dyspnea on the least exertion and of edema of the lower extremities.

Examination.—Physical examination disclosed that he weighed 150 pounds (68 Kg.), was 63 inches (160 cm.) in height and had a blood pressure of 185 systolic and 90 diastolic and a pulse rate of 72 beats per minute. Tenderness in the hepatic and renal regions, marked edema of both lower extremities and dyspnea were also noted. Fluoroscopic examination showed that the aortic arch measured 9 cm. in width, and the distance from the apex to the approximate base was 21 cm.

Chemical examination of the blood showed: sugar, 220 mg.; cholesterol, 198 mg.; uric acid, 4 mg., and urea nitrogen, 29.4 mg. per hundred cubic centimeters of blood. The quantities of these substances were high, since the sugar content is normally between 60 and 120 mg., that of cholesterol between 160 and 180 mg., that of uric acid between 1 and 3 mg. and that of urea nitrogen, between 12 and 15 mg. per hundred cubic centimeters. Urinalysis revealed sugar, a large amount of albumin and some hyaline casts.

Course.—After three months of treatment, there was a prompt subsidence of all symptoms, and the fluoroscopic examination showed an aortic width of 7 cm. and an apex to base measurement of 19.5 cm., each evidently undergoing an approximate reduction of 2 cm. The tumors in the skin presented little change. The patient claimed that they were present before the onset of the diabetes, and were noted by him at the time of his attack of acute nephritis.

Case 4.—Mrs. G. was not diabetic, but presented signs of arteriosclerosis; she had a number of growths of the xanthoma planum variety on both palpebral regions.

SUMMARY

1. A case of xanthoma tuberosum with extensive involvement of the tendons, in which the planum variety of lesion was also seen, is presented.

2. The sugar, cholesterol and nonprotein nitrogen contents of the blood of this patient were higher than those found in the normal person.

3. The presence of the same type of lesion in the tendons of a brother and of other relatives, a negative Wassermann reaction of the blood and the absence of evidence of other infectious diseases suggest a hereditary tendency.

4. The characteristics of xanthoma as exhibited by xanthoma cells, fibroblastic reactions, deposits of lipoid material, degenerated muscle cells and the resemblance to a malignant condition are presented in the histopathologic studies.

5. Chemical analysis of the blood in two cases revealed cholesteremia, glycemia and a rise in the nonprotein nitrogen. The last has not heretofore been reported in connection with this disease.

6. In two of the cases there was no rise in the sugar content of the blood above normal, and the urine was free from sugar.

7. In three of the cases, including two of those previously mentioned, there was definite evidence of arteriosclerosis. The relation between arteriosclerosis and xanthoma tuberosum has not been observed heretofore.

8. In the third case, there were hypertension and nephritis, primarily, and diabetes secondarily related to the xanthoma tuberosum.

MODERN INTERPRETATION OF MYCOTIC INFECTIONS OF THE FEET AND HANDS

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Modern dermatologic investigation has lifted epidermophytosis from the rôle of a purely local skin disease to that of a skin-sensitizing agent, with a probable influence on the life cycle and habits of the skin.

The ringworm fungi located in the interspaces of the toes and on the soles of the feet are favored by those elements essential to undisturbed growth, such as heat and moisture, as well as by their inherent and enormous powers of spread and multiplication, their prolonged and hardy life, and their tendency toward a resting spore stage of indefinite duration and latent virulency, even under adverse circumstances.

Reasoning from cause to effect is a logical procedure in investigation. In epidermophytosis, with definite knowledge of the cause, attention is naturally focused on the study of the effect, i. e., the produced pathologic picture. These pathologic changes have been studied by a number of observers, and, according to Peck,[1] their observations have been summarized by Miescher, to whom we are indebted for the facts given under the following heading.

THE PATHOLOGIC PICTURE

Epidermophytosis of the extremities presents two main clinical types, an acute vesicular form and a subacute or chronic hyperkeratotic form. Therefore, the pathologic pictures presented are those of vesicular mycotic lesions and squamous mycotic lesions. Broadly considered, there is little that is basically different in these two varieties, the greatest variation being one of degree of intensity. In both forms, the ringworm fungi are found resident, for the most part, in the upper two thirds of the stratum corneum, and also as far down as the stratum

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From the Dermatologic Clinic and the Research Laboratories of the Skin and Cancer Hospital of Philadelphia, Albert Strickler, M.D., medical director.

1. Peck, S. M.: Epidermophytosis of the Feet and Epidermophytids of the Hands: Clinical, Histologic, Cultural and Experimental Studies, Arch. Dermat. & Syph. **22**:40 (July) 1930.

granulosum—always among the partially or completely cornified cells, parallel to the surface, segmented and containing granules. In spite of this apparently harmless location, the presence of ringworm fungi results in inflammatory changes not only in the living layer of the epidermis, but also in the true skin.

In the vesicular mycotic lesions, the irritant is so intense as to cause an intracellular edema and spongiosis of the cells of the prickle cell layer. The resultant vesicles have walls formed by the surrounding epidermis and a roof consisting of the stratum corneum alone or with the addition of a few layers from the stratum granulosum, and surrounding these vesicles there are collections of polymorphonuclear leukocytes. The contents of the vesicles consist of fibrin, polymorphonuclear leukocytes and epithelial cells in various stages of degeneration. In the cutis vera, there is a cellular exudate consisting of polymorphonuclear cells and lymphocytes, usually most marked in the papillary and subpapillary layers directly beneath the vesicles. The blood vessels are dilated and show infiltration by the same type of cells; there is some increase of fibroblasts. The sweat glands in the affected area appear normal. Fungi have been found only in the sections taken from the plantar surface.

In the squamous mycotic type, the effect of the offending cause seems to be less intense, but evidently of greater persistency. The vesicular features are here represented by microscopic subcorneal vesicle formation, with abortive lesions of the same character in the stratum malpighii. Here the process begins rather deeper than in the vesicular mycotic lesions, i. e., in the basal and overlying layers. This variation between the vesicular and squamous mycotic lesions has a clinical bearing on the rapidity of cure, to which attention will be called in another communication.

THE PROBLEMS PRESENTED

In the broad conception of this disease, the lesions that these ringworm fungi produce between the toes and on the feet are to be regarded as in the nature of local foci wherein the fungi live and multiply. The relationship of the fungi, so located, to those distal lesions regarded as being the result of the same etiologic factor as the lesions on the feet, as well as the possible effect of the hyphomycetes on the general cutaneous surface, is a problem toward the solution of which we hope to contribute additional information. Study of this problem presents a number of pertinent questions, as follows:

Are the local pathologic changes of epidermophytosis of a purely mechanical nature, or are they the result of metabolic (toxic) materials elaborated by the fungi after they gain entrance? If this is so, is it probable that these toxic metabolic materials enter the general circula-

tion, sensitizing the cutaneous surface and preparing the skin for the development of secondary dermatoses? Is it possible for the mycelia, in any form, to gain entrance into the general circulation and, localizing, produce cutaneous disease? Are the secondary eruptions the result of a sensitization of the skin by ringworm metabolic toxins plus irritants of internal or external origin, or is it a question of transference through contact or of extension through tissue continuity? What evidence can be submitted to justify the adoption or the rejection of any of these hypotheses? The following pages will be devoted to an effort at solving the propounded questions.

THE INVESTIGATIVE APPROACHES

Absence of anything really distinctive in the microscopic picture of these mycotic lesions removes, at least partially, one important avenue of investigation. Except for the presence of fungi in the nonliving portion of the skin (toes and plantar surfaces only) and perhaps for the fact that leukocytic infiltration in the epidermis is seen earlier and forms a more striking picture, there is nothing pathologically distinctive between these lesions and corresponding lesions caused by many external factors (dermatitis venenata, occupational dermatoses, etc.).

However, the presence of these fungi within the skin—true, only within the nonliving portion—calls for a consideration of the life cycle and habits of these hyphomycetes, with the hope of thus shedding light on these problems. It is very apparent from the ability of these fungi to live among the cornified structures of the skin, from their ability to grow and develop at the variations of room temperature outside the body, and from their aptitude to go into an apparent saprophytic existence for a considerable period of time, with potential powers of assuming pathogenic rôles when the environment is favorable, that these organisms belong to a rather hardy stock (mycologic perennials). However, these fungi undoubtedly have their metabolic problems at all times and under all circumstances.

It is known that in the test tube, for instance, ringworm fungi need for growth and development a source of carbon, a source of nitrogen and a medium of low p_H. These conditions are most admirably fulfilled in the culture medium known as "French proof agar," in which the ringworm fungi grow most luxuriantly. Sabouraud was probably among the first to observe that ringworm fungi can grow on agar peptone medium, but with increased luxuriance of growth only after the addition of sugars. Various synthetic mediums composed of inorganic salts have been devised for the growth and study of yeasts, and some of these have been adopted experimentally for the growth of the ringworm fungi. These synthetic mediums contain, principally,

either phosphates or lactates. Weidman and Spring,[2] as a result of their investigations with such mediums, concluded that phosphates are conducive to the development of spores in increased ratio to mycelia, but that an excess of lactates favors the growth of mycelia over the production of spores. These authors drew up the following hypothesis relative to spore formation. As long as a colony grows rapidly and the food supply is abundant, no spores form. The important function of a colony seems to be the development of mycelia (vegetative function), and this continues until famine or some other adverse condition arises. Then the reproduction phase is taken care of, and the development of spores begins.

In this connection, certain experiments conducted in the laboratories of the Skin and Cancer Hospital of Philadelphia seem worthy of mention.

Two grams of psoriasis scales was washed with ether to remove the lipoids, and after evaporation of the ether 50 cc. of a 10 per cent solution of sodium hydroxide was added and the mixture warmed gently. Practically all of the material dissolved. The mixture was filtered, and on neutralization with concentrated hydrochloric acid a white precipitate formed. This was filtered again. This filtrate has been termed skin solution. In addition, a mineral solution was prepared, combining potassium phosphate, potassium chloride and magnesium phosphate.

A flask containing 10 cc. of skin solution plus 1 Gm. of dextrose plus 40 cc. of mineral solution plus Trichophyton cerebriforme culture gave excellent growth.

A second flask containing no skin solution but containing 1 Gm. of dextrose plus 50 cc. of mineral mixture plus Trichophyton cerebriforme culture gave excellent growth.

A third flask containing 10 cc. of skin solution but no dextrose, plus 40 cc. of mineral mixture plus Trichophyton cerebriforme culture yielded a growth about one-tenth as intense as that in the first and second flasks.

A fourth flask containing 20 cc. of skin solution plus 30 cc. of water, but no dextrose or mineral mixture, plus Trichophyton cerebriforme culture yielded very slight growth.

A fifth flask containing 1 Gm. of dextrose plus 50 cc. of mineral mixture, but no skin solution, plus Trichophyton cerebriforme culture gave good growth, but less than that in the first and second flasks.

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2. Weidman, F. D., and Spring, Dorothy: Comparison of Ringworm Culture Ingredients: II and III, Arch. Dermat. & Syph. **18**:829 (Dec.) 1928.

In the first, second and fifth flasks, the characteristics of the growth bore a striking resemblance to the growth of the same type of fungus on Sabouraud's medium.

A comparison of conditions outside the body with those that ringworm fungi encounter when entering within the skin is most instructive. A chemical analysis of human epidermal scales shows 12 and 14 per cent nitrogen, an amount more than sufficient to maintain the absolute life necessities of ringworm fungi (spore existence). During these lean periods, the hyperkeratosis and sogginess of the interspaces so frequently encountered in the silent forms of epidermophytosis probably not only contribute protection against the normal rate of exfoliation, but also serve as a reservoir or backlog of food supply. The prevalence of the silent form of ringworm infection of the feet may be gleaned from an unpublished report [3] dealing with a study of 1,073 consecutive outpatient cases in the Skin and Cancer Hospital of Philadelphia. In this series, 529, or 51.7 per cent, were found to be of the asymptomatic (silent) type, and only 50, or 4.7 per cent, symptomatic. Of the asymptomatic group, 62 per cent showed soggy, macerated, more or less thickened epidermis (intertriginous type); 17.2 per cent dry, scaly, hyperkeratotic lesions, and 20.8 per cent no demonstrable clinical pathologic condition. Statistics giving practically the same percentages have been reported by White [4] and Legge, Bonar and Templeton.[5]

This behavior of the ringworm fungi within the body is comparable to that on the agar peptone medium of the test tube and in the skin and mineral solutions of the experiments detailed. That the skin can and does adjust itself to such alterations in its chemistry as to create a favorable soil for a luxuriant growth of ringworm fungi, whereby these hyphomycetes develop in a manner comparable to their growth on Sabouraud's medium, thus giving life to the symptomatic clinical variety of epidermophytosis, rests on the following facts: 1. Recent laboratory evidence seems to point to the skin as a temporary storehouse for large amounts of dextrose. 2. A fairly constant ratio between the dextrose content of the skin and that of the blood is maintained, excepting when large amounts of dextrose are ingested. 3. The skin contains diastatic and glycolytic enzymes. 4. A specific carbohydrate metabolism of the skin may be observed experimentally. 5. Lactic

3. Strickler, Albert, and Friedman, Reuben: Ringworm of the Feet—Symptomatic and Asymptomatic, Arch. Dermat. & Syph. **24**:430 (Sept.) 1931.

4. White, C. J.: Fungus Diseases of the Skin: Clinical Aspects and Treatment, Arch. Dermat. & Syph. **15**:387 (April) 1927.

5. Legge, R. T.; Bonar, Lee, and Templeton, H. J.: Ringworm of the Feet, J. A. M. A. **92**:1507 (May 4) 1929; Incidence of Foot Ringworm Among College Students: Its Relation to Gymnasium Hygiene, ibid. **93**:170 (July 20) 1929.

acid [6] is an important product of carbohydrate metabolism, and is normally present in the skin. 6. The presence of dextrose in the incubating medium, especially in a phosphate buffer solution, increases the formation of lactic acid. 7. Increased amount of sugar in sweat creates a more favorable environment for the growth of fungi.[7]

The conditions outlined are all that are necessary for the full growth and development of any ringworm fungi present within the skin structures. The problem remaining is the determination of the ways and means whereby these hyphomycetes utilize these products.

Anatomically, the sweat glands appear as the only suitable carriers for this rich pabulum, for the absence of a limiting wall when they are traversing the epidermis permits a most intimate contact between the secretory fluid (sweat) and those epidermal cells that are the residential seat of the ringworm fungi.

In this mycotic disease, the sweat glands do not show any pathologic changes, but rather an increased physiologic activity—nature's compensatory method—an associated hyperhidrosis due to the inability of the sudoriferous glands to excrete waste products in concentration. This localized sweating, with a similar condition of the hands frequently encountered in epidermophytosis and epidermophytid conditions, often signalizes the growth and spread of the ringworm fungi within the affected structures, adding its increased toxic metabolic products to the eliminative burden of these sweat glands. This hyperhidrosis often markedly diminishes coincident with clinical improvement, and in our experience its diminution is often indicative of an abatement in the activity of the hyphomycetes.

With conditions within the skin comparable to those that in the test tube favor the unfettered (mycelial) growth of the ringworm fungi, it would require but little to set off the spark that would result in an acute inflammatory process of the invaded skin structure. Whether excessive perspiration with its irritant excretory products or the toxic metabolic products of the fungi, or both of these factors plus some form of trauma, are necessary to produce the clinical vesicular lesions of symptomatic epidermophytosis is difficult to say. However, it is certain that excessive hyperhidrosis must play some part in the production of the cellular spongiosis, important as a factor in the pathologic picture of symptomatic mycosis.

The presence of this acute inflammatory process within the skin, with increased vascularity, spongiosis of epidermal cells, increased and abnormal metabolism and hyperphysiologic hyperhidrosis, no doubt

6. Pillsbury, D. M.: The Intrinsic Carbohydrate Metabolism of the Skin, J. A. M. A. **96**:426 (Feb. 7) 1931.

7. Usher, B.: Bactericidal Properties of Human Sweat, Arch. Dermat. & Syph. **20**:665 (Nov.) 1929.

places an entirely new aspect on the life cycle of the involved cutaneous structures. In the bedlam thus created, it is possible, and indeed probable, that the permeability and the osmotic properties of the vascular and lymphatic channels are so altered as to permit entrance not only of mycotic toxic products, but possibly of the hyphomycetes themselves into the great transportation system of the body.

Affinity of bacteria for certain organs and structures of the body is an established fact, and a similar relationship, no doubt, must exist between pathogenic hyphomycetes and the human structures. Affinity of ringworm fungi for the epidermis and its appendages, the hair and the nails, is recognized. Theoretically, it is fair to assume that the toxic products elaborated by these fungi are dermatotropic, expressive of the peculiar affinity of these hyphomycetes. In line with the same reasoning, it is logical to assume that absorption of these toxic products by any epidermal structure renders that structure trichophytin-sensitive. Proof that this theoretical concept has its counterpart in reality is found in positive reactions to specific cutaneous tests and in human inoculation experiments.

In a series of twenty-three cases of epidermophytosis of the feet and epidermophytids of the hands, Peck found that all the patients gave positive reactions to the endermic trichophytin test. In 1929, Jadassohn and Peck [8] reported a series of twenty-four cases of mycotic infection of the feet associated with dyshidrotic and scaly conditions of the hands in each of which there was a positive reaction to trichophytin. Similar results have also been reported by Walthard.[9] Sulzberger and Lewis [10] recently devised a contact test to measure sensitivity to trichophytin. The conclusions given in their preliminary report may thus be summarized: "The test was frequently positive in patients with either tinea or a history of tinea and negative in those who showed no clinical evidence of fungus infection or without history of such infection. Different parts of the body in the same patient gave different results; frequently the hands were found no more sensitive than other parts."

Further proof that trichophytin skin sensitivity occurs is to be gleaned from the auto-inoculation dermatophytosis experiments of Cleveland White.[11] This author inoculated four persons experimentally

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8. Jadassohn, W., and Peck, S. M.: Arch. f. Dermat. u. Syph. **158**:16, 1929.

9. Walthard, B.: Zur Pathogenese des dysidrotischen Symptomen Komplexes: Ueber ein unter dem Bilde einer Dysidrosis verlaufendes Epidermophytid, Dermat. Ztschr. **53**:692 (April) 1928.

10. Sulzberger, M. B., and Lewis, G. M.: Trichophytin Hypersensitiveness Demonstrated by Contact Tests, Arch. Dermat. & Syph. **22**:410 (Sept.) 1930.

11. White, Cleveland: Auto-Inoculation Dermatophytosis from Toe Cultures of Human Volunteers: Clinical, Laboratory, Experimental and Therapeutic Studies in Superficial Mycotic Dermatitis, Arch. Dermat. & Syph. **20**:315 (Sept.) 1929.

with fungus cultures and positive fungus scrapings. A detailed history of two of these volunteer subjects is furnished; both suffered from dermatophytosis of the feet. In these inoculation experiments, cultures from the patient's own toe were used; the back was the area selected for inoculation in each case, and at times, the axilla. Positive "takes" were noted in from three to four days after the implantation of the cultures, and it took from ten to sixteen days for the hyphae to disappear from the lesions. The lesions were mainly erythematous and lasted about from three to four weeks. Secondary inoculations gave the same results as the primary.

Experimental proof of the ability of the ringworm hyphomycetes to establish a fungus focus in human interspaces has been furnished by the researches of Peck.[1] A summary of his experiments, in substance, follows:

The human subject chosen was free from clinical epidermophytosis of the feet and gave a negative reaction to trichophytin. Mycosis of the foot was produced through the application of a 3 weeks old culture of Epidermophyton Kauffman-Wolf, previously isolated from mycosis of the feet. The culture plus a portion of Sabouraud's medium was placed between some of the toes, kept in close contact with adhesive tape. The whole foot was wrapped in a thick flannel cloth and bandaged. The month was July, and it was hot; the patient was encouraged to walk as much as possible. In this experiment, all conditions favorable for a "take" were carried out. Four days after the beginning of the experiment, vesicles and pustules appeared on the treated parts of the foot, and the lesions were microscopically positive for ringworm fungi.

On the fifth day, the lesions on the foot reached their height, and in two months these eruptions healed spontaneously. Fungi could be demonstrated microscopically for a week after the first appearance of the eruptions, and cultures made from scales and vesicles at this time yielded a growth of Epidermophyton Kauffman-Wolf in almost every tube. Thirteen days after the beginning of this experiment, the reaction to trichophytin became positive, and its positiveness continued to increase in intensity for some days, not disappearing even at two months. Twenty-four days after the beginning of this experiment, a few dyshidrotic vesicles appeared on the fingers of the right hand. During the next two weeks, a few scattered, deep-seated vesicles appeared in crops on both hands and disappeared without visible desquamation. The lesions on the hands were negative for fungi.

As soon as the clinical lesions healed, and while the reaction to trichophytin was still positive, the foot of the patient was reinfected with a three weeks culture of Epidermophyton Kauffman-Wolf isolated previously from this case. The infection was characterized by a greater degree of inflammation. The eruptions on the foot reached their height about the sixth or the seventh day and presented the appearance of a typical intertriginous vesiculopustular mycosis of the foot. Fungi could be demonstrated microscopically and culturally sixteen days after the onset of the experiment. Two weeks after the beginning of the experiment, a generalized dyshidrotic eruption appeared on both hands, which clinically and histologically could not be differentiated from the nonexperimental clinical epidermophytid infection. The eruption remained on the hands for eight days and disappeared with desquamation. The lesions on the hands were microscopically and culturally nega-

tive for fungi. The reaction to trichophytin was, at the end of this experiment, still strongly positive.

BLOOD CULTURE STUDIES

With definite knowledge that absorption of toxic products of the fungi takes place, attention is now focussed on the rôle that the fungi themselves assume, and especially on the possibility of their entrance into the blood stream.

The first reported case of ringworm fungi in the blood stream of a patient suffering from epidermophytosis of the feet and epidermophytid of the hands was that of Peck.[1] The following is a brief summary of the case:

A boy, aged 18, suffered for four weeks with a mycosis of both feet, partly intertriginous and partly vesiculopustular. Microscopic examination of the lesions of the feet showed fungi. Clinically, the hands presented a generalized dyshidrotic eruption, with scattered pustules and confluent vesicles on the fingers and hands, as far as the wrist. Repeated search, both microscopic and cultural, for fungi in the lesions on the hands, yielded only negative results. The reaction to trichophytin was strongly positive. Two hours after this cutaneous test, blood cultures were made with Sabouraud's maltose agar. On one of the blood plates, a growth of ringworm fungus appeared, similar to that obtained through culture of the lesions on the feet.

About ten months ago, and without knowledge of the work of Peck, the Research Staff of the Skin and Cancer Hospital of Philadelphia undertook blood culture studies of patients suffering with mycotic conditions of the feet. In all, 290 blood cultures were made from that many patients, with 3 positive findings. The case histories of the patients whose blood yielded the fungi follow:

Case 1.—A. M., aged 29, came to the hospital with an eruption involving the hands and the plantar aspects of both feet of five years' duration. Clinically, the right hand showed patches of exfoliation with definite margination and slight undermining of the epidermis. There were eight patches in all, with three on the dorsal surface of the hand from the second phalanx to the tips of the fingers. The left hand showed the same picture, except that the lesions were less numerous and less marked. The right foot showed slight scaling between the toes, and on the plantar aspect, between the heel and the ball, there was a poorly marginated patch of hyperkeratosis. The left foot presented about the same picture as the right. The itching of both hands and feet was rather intense. The diagnosis of epidermophytosis of the feet and epidermophytid of the hands was made. Ringworm fungi were found in the material taken from between the toes and from the lesions on the plantar aspects, both by microscopic examination and on culture. The hands were repeatedly negative for ringworm fungi.

Two days after the first visit, three blood cultures were made on Sabouraud's medium. On the sixth day, typical ringworm colonies appeared; these were subcultured and presented the typical picture of Trichophyton gypseum.

Case 2.—R. Dev., aged 39, came to the Skin and Cancer Hospital complaining of an eruption involving almost the entire arm of one week's duration. The lesions

consisted of small pinhead-sized discrete papules of a rather subdued red color. The condition was associated with some itching. The right foot showed some scaling and exfoliation of all the interspaces, and the left presented the same picture, excepting that it was more marked. Microscopic examination of the scrapings from the interspaces disclosed hyphae and spores in abundance, while scrapings from the papular eruptions proved negative for ringworm fungi. Epidermophytosis of the feet and lichen trichophyticus of the arms were the diagnoses made.

Cultures of the material from the interspaces were made on Sabouraud's medium and showed a growth of ringworm fungi. Four days after the initial visit, three blood cultures were made on Sabouraud's medium. Microsporon radians-concentricum was isolated in pure culture.

CASE 3.—G. M., aged 19, consulted one of us (A. S). for an eruption on the plantar surface of the right foot of five years' duration. The entire foot was moist.

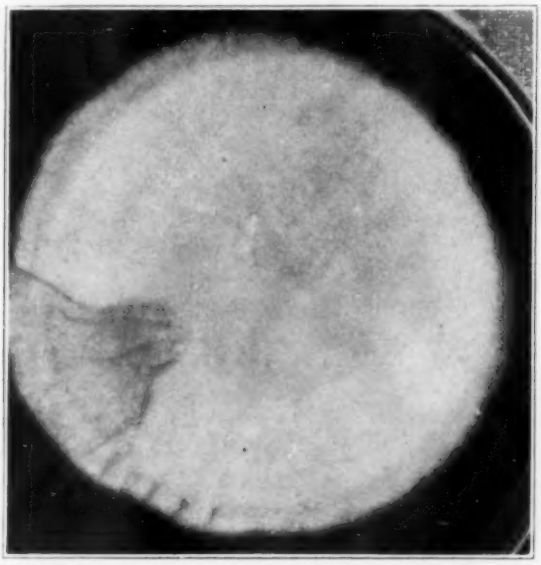

Fig. 1 (case 1).—Trichophyton gypseum (from a blood culture).

Examination showed grouped, steel-colored, rather superficial, vesicular lesions, irregularly scattered over the affected plantar surface, with extension to the inner and outer sides of the foot. Similar lesions were seen on the plantar aspect of the toes, while the interspaces, especially the third and fourth, showed marked sogginess of the epidermis. The hands were free from eruptions.

Microscopic examination of the tops of the vesicles showed numerous interlacing mycelia. Scrapings from the hands were negative for fungi. Culture of the vesicular material on Sabouraud's medium proved negative for ringworm fungi. About four months after beginning treatment, three blood cultures were made, which were identified as Trichophyton cerebriforme.

The following experiments on animals were undertaken with the cultures from these cases:

EXPERIMENT 1.—The abdomens of one rabbit and three guinea-pigs were shaved, epilated and gently rubbed with sandpaper. A three to four week culture of Tri-

chophyton gypseum (case 1) was rubbed lightly into the shaved and abraded skin according to the technic of Bruno Bloch.

For the first five days the treated skin showed only the evidence of a traumatic reaction. On the seventh and eighth days there was marked scaling with diffuse infiltration of the surrounding skin. On the ninth day the inflammatory symptoms increased; the acme was reached on the twelfth day. At this time the infected part of the abdomen was covered with dark brown, crustlike scales and showed evidences of infiltration. The animals appeared sick, were very quiet in their cages and refused food. After from three to four days the general condition of the animals changed, the inflammatory signs disappeared, and the animals recovered quickly.

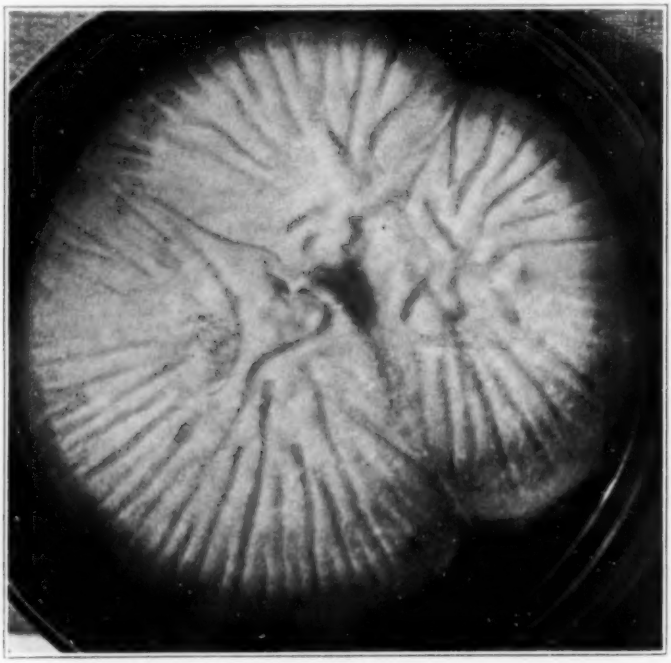

Fig. 2 (case 3).—Trichophyton cerebriforme (from a blood culture).

Microscopic examination of the crustlike scales showed ringworm fungi in great number.

An attempt was made to recover the organism from the blood of these animals, the technic of Jadassohn being used. Blood was obtained through puncture of the hearts of these animals and added in amounts of from 1.5 to 2 cc. to each tube of liquefied Sabouraud's medium. Fungi were recovered from the blood of guinea-pig 1, withdrawn two hours after infection. No growth was obtained from the blood of guinea-pig 2, withdrawn fourteen hours after infection, or from that of guinea-pig 3, cultured ten hours after infection. Fungi were recovered from the blood of rabbit 1, which was taken from the heart, one hour after endermic infection.

EXPERIMENT 2.—In a second experiment, only two guinea-pigs were used, each being infected endermically and intracardially with Trichophyton cerebriforme (case 3). The course of the disease in these animals corresponded to that seen

in experiment 1. The trichophyton fungi were demonstrated in the scales and recovered by culture on Sabouraud's medium. The acme of the infection was reached on the eleventh day. Blood cultures taken during the acme period were found negative for fungi.

In this connection, the researches of Sulzberger[12] offer confirmatory evidence of value. This investigator undertook a problem involving endermic infection of guinea-pigs with Achorion quinckeanum and the making of subsequent blood cultures at various intervals. His comments, in substance, will be given:

1. Following the cutaneous infection of guinea-pigs with Achorion quinckeanum, fungi could be cultured from the blood at various times.

2. There were three phases to this experimental blood stream infection, two positive and one negative. In the first positive phase, fungi were demonstrable in the blood stream from one to two hours after cutaneous infection; this was followed by a negative phase varying in duration from three to nine days; then came a second positive phase from ten to eleven days after infection, in which fungi in large numbers could be demonstrated in the blood stream through culture.

3. Bruno Bloch and others have shown that the second positive phase corresponds to the acme stage of the primary lesion, when allergy is at its maximum.

4. It is still an open question how far these experiments on animals apply to trichophytic infections in man.

SUMMARY

1. Mycotic infection of the feet, in the light of the new conceptions, can no longer be regarded as only a local skin condition.

2. The lesions of epidermophytosis of the feet are to be regarded as local foci, from which, under certain conditions, absorption of toxic substances (fungus, metabolic or both) can take place.

3. These substances are dermatotropic, acting as skin-sensitizing agents and playing a rôle in the causation of various secondary (mycid) eruptions.

4. Comparable to this trichophyton fungus phenomenon, mention can be made, for instance, of bacteria that, locked up in various organs, act as local foci of infection and play at times an important etiologic rôle in such dermatologic diseases as chronic urticaria, erythema nodosum, erythema multiforme, etc.

5. To a degree, considerable similarity exists in origin and behavior between the secondary cutaneous conditions due to ringworm fungus

12. Sulzberger, M. B.: The Pathogenesis of Trichophytids: The Spontaneous Passage of Formed Elements (Spores) from the Primary Lesion into the Circulating Blood, Arch. Dermat. & Syph. **18**:891 (Dec.) 1928.

(epidermophytids and trichophytids) and certain of the tuberculids and secondary syphilitic eruptions.

In the tuberculids, the primary focus is often both insignificant and concealed, a situation in part comparable to the primary focus in epidermophytid infection of the hands. In both of these cutaneous conditions, the secondary eruptions are often clinically the most prominent, the most widespread and of the greatest significance.

In syphilitic infection, the primary lesion is rather easily recognized as a rule, and usually leaves an imprint on the involved structure. However, with all its importance, it is overshadowed by the secondary eruptions in which the situation becomes comparable to that of the secondary ringworm fungus cutaneous involvement. In both the tuberculids and the secondary syphilitic dermatoses, skin sensitization plays an important etiologic rôle, comparable, it is our belief, to that observed in the trichophyton fungus infections under consideration.

6. In trichophyton fungus infections in man and in experimental trichophyton fungus infections in animals, ringworm fungi have been found in the blood stream. It appears more than probable that the fungi in the human infections are destroyed rather quickly and early, possibly in the lymphatic channels or in the lymphatic glands, and that their main function probably consists in augmenting in some manner the cutaneous sensitizing influence of the hyphomycetic products. That the lymphatic channels can shield and transport ringworm fungi is paralleled by a similar relationship known to exist between the lymphatic vessels and spirochetes.

7. The following important practical deductions may be drawn from a survey of the literature and the additional experiments cited:

(*a*) In the treatment for the chronic recurrent epidermophytosis of the feet and epidermophytid eruptions of the hands, desensitization of the skin through trichophytin therapy would seem a logical procedure.

(*b*) There is urgent necessity of some form of cutaneous test of just sufficient sensitivity to serve as a reliable and specific diagnostic aid in the etiologic determination of the various squamous and vesicular eruptions of the hands and lichenoid eruptions of the extremities.

(*c*) Complement-fixation or related serologic studies are advisable as a means of shedding more light on the nature of the sensitizing influence of the mycotic infections of the feet, and possibly also as a diagnostic procedure.

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TRIETHANOLAMINE: AN ADJUNCT TO DERMATOLOGIC THERAPY

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Dermatology has made little use of organic chemistry as compared to the use made of it in industry. With the exception of a few of the complex acids and the arsenical groups, dermatologists are content with the more or less galenic combinations of iodine, sulphur, tar and the simple vehicles. One does not realize the immensity of the field in commercial organic chemistry until one discusses the problem with a progressive organic chemist.

About one year prior to the writing of this paper, I had the opportunity to discuss with a chemist connected with a large chemical corporation the problem of the penetration of drugs and their vehicles into the skin. I had in mind mainly the control of the deeper-growing fungi by means of therapy with drugs of deeper penetration.

At that time he suggested that I investigate a preparation called triethanolamine. I obtained a sample of this preparation through the courtesy of the Carbide and Carbon Chemical Corporation of New York, and found that it was not only an excellent penetrant of organic material, but that it was also possessed of other properties that will probably open up a considerable field for its use among dermatologists.

Though I have used the preparation for a year, this article can be hardly more than a preliminary report. The opportunity to observe its action in a large series of selected cases in various combinations can come only through considerable experience with its many phases. The product is reported here in a relatively limited number of preparations mainly to interest other workers in its use in the hope that the field may be more rapidly extended.

The following statement of its physical and chemical properties is a quotation from a pamphlet of the Carbide and Carbon Chemical Corporation.

> Triethanolamine is a colorless, viscous liquid with a slight ammoniacal odor. It boils at 277 to 279 C. at 150 mm., has a specific gravity of 1.1242 at 20 to 4 C. and is extremely hygroscopic. It is entirely soluble in water in which it gives a strongly basic reaction.

Submitted for publication, May 21, 1931.
Read before the Dermatology and Syphilology Section of the California Medical Association, at the Sixtieth Annual Session, San Francisco, April 27, 1931.

The commercial product contains approximately 75 per cent triethanolamine, 20 to 25 per cent diethanolamine and 0 to 5 per cent monoethanolamine. Since the properties of the ethanolamines are very similar, consistent results can be obtained by the use of a mixture of definite composition. Small quantities have been found to increase markedly the penetration of various oily materials. For example, the addition of one-half to one per cent of triethanolamine to creosote will very markedly reduce the time of its penetration into various kinds of wood. In general, triethanolamine may be said to increase the penetration and adhesion of liquid in or to a porous material.

The ethanolamines combine with fatty acids to form soaps with most valuable characteristics. These soaps are soluble not only in water, but also in gasoline, kerosene and oils. They possess excellent detergent properties, and may be incorporated in facial creams or shaving soaps yielding a cream which can be completely removed by washing with water. Small amounts of ethanolamine soaps may also be used to emulsify oil or water for the preparation of cutting compounds and similar emulsions.

Table Showing Comparison Between Penetrating and Antiseptic Powers of Triethanolamines and Those of Phenol

Monoethanolamine, Sample Marked	Diethanolamine, Dilution	Triethanolamine, Distance from Cup Showing No Growth		Effect on Blood Serum and Agar:
		Cm.	Subsurface	Surface
250,749 monoethanolamine	Straight	1.8	2.2 cm. (colonies small)	None
	1:3	1.6	2.0 cm. (colonies small)	None
250,750 diethanolamine	Straight	1.3	2.0 cm. (colonies small)	None
	1:3	0.9	1.5 cm. (colonies small to 2.5 cm.)	None
250,751 triethanolamine	Straight	0.8	1.4 cm. (colonies small to 2.3 cm.)	None
	1:3			
Phenol	1:20	0.4	0.5 cm.	None
			0.6 cm.	None

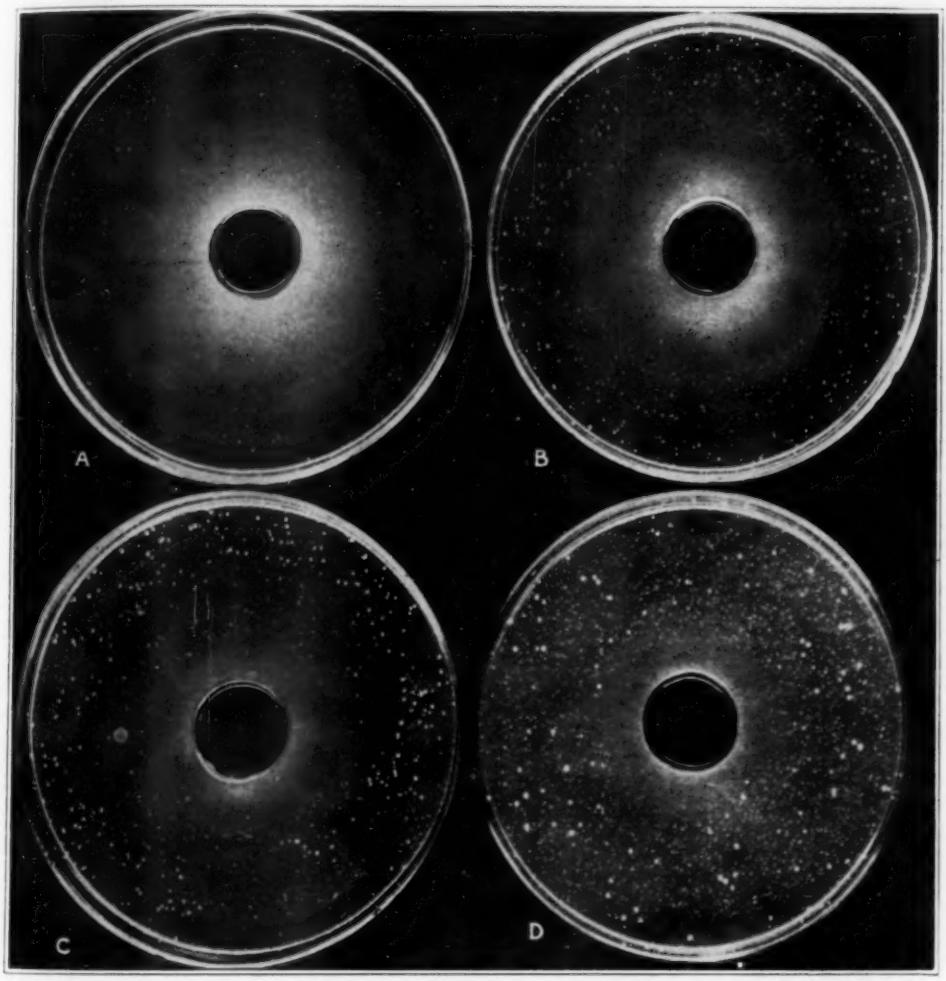
The ethanolamines are among the most hygroscopic liquids known, absorbing approximately twice as much water as glycerin. Their use as softening and moistening agents is consequently assured.

I have likewise been furnished a report by the Pease Laboratories, Inc., of New York, on the antiseptic action and penetrating power of triethanolamines. In this a comparison was made between the penetrating and antiseptic power of triethanolamines and those of phenol. The results are shown in the accompanying table. They are perhaps more graphically shown in the laboratory photographs.

Since it might be argued that the action shown may have been due to the hydrogen ion concentration, the tests were repeated in the same laboratory with sodium hydroxide instead of triethanolamine; no inhibition of colony growth due to this base was reported.

Thus the preparation is a liquid, glycerin-like substance with strongly basic properties; it has a remarkable power of increasing the penetration of oily substances and, in addition, a certain amount of bacteriostatic action.

The next consideration must be as to whether or not such a preparation can be used safely on normal or pathologic skin. As a test, I applied undiluted triethanolamine to a raw granulating surface, covering a large portion of the back of a hand. No discomfort was complained



A, 250,749 monoethanolamine, straight B. E. agar plus 10 per cent horse serum; incubated broth culture (I.B.) of Micrococcus aureus. *B*, 250,750 triethanolamine, straight, beef extract (B.E.) agar plus 10 per cent horse serum; Micrococcus aureus (I.B.). *C*, 250,751 triethanolamine, straight, B. E. agar plus 10 per cent horse serum; Micrococcus aureus (I.B.). *D*, phenol (1:20), B. E. agar plus 10 per cent horse serum; Micrococcus aureus (I.B.).

of by the patient, except a slight drawing sensation for from six to seven hours after application. The preparation was applied repeatedly,

and at the end of one week no appreciable irritation of the healing areas was noted. There was also no retardation of epithelial growth. The preparation served as an excellent compress medium, as it did not dry out. There were no general toxic effects.

A similar lack of irritation was noted in all therapeutic combinations of the chemical. However, it did accentuate the action of those substances for which it proved to be a solvent.

I have used the preparation therapeutically in the following ways: As a vehicle for salicylic and benzoic acids, in the proportions used in Whitfield's formula. This was not particularly desirable, because it was too difficult to limit the distribution of the preparation to the treated area. As a constituent in Whitfield's ointment, it produced a more rapid keratolytic action, so that it was desirable to reduce the salicylic acid. In the use of oily substances in the scalp, it has proved invaluable from the standpoint of easy removal. This holds true for petrolatum vehicles or for oily therapeutic agents, such as oil of cade.

The following formula has proved excellent in the control of seborrhea of the scalp: oil of cade, 24, triethanolamine, 4, and liniment of soft soap, U. S. P., 120. Without the triethanolamine, this preparation is extremely hard to remove. With the chemical, it washes out at once. My instructions to the patient are to leave the preparation on for three hours before the hair is washed.

A third important use has been its combination with iodine in the treatment for ringworm infections of the scalp. The following formula has been repeatedly used with excellent success: iodine crystals, 4, triethanolamine, 2, and enough goose grease to make 30. This should be prepared by mixing the goose grease and the triethanolamine and then adding the iodine. This mixture slowly elaborates free iodine and gradually turns from a brownish mixture to one that is colorless. If the iodine and triethanolamine are mixed first, a rapid elaboration takes place, robbing the preparation of this reaction. In the few cases of ringworm of the scalp in which I have had the opportunity of using it, the treatment interval has been reduced markedly. Only one of the patients showed possible evidence of disease after four weeks of its use. Since the preparation has been employed in only five cases, this statement is of course entirely indeterminate. The resistant case was one of small-spored ringworm and was of three years' duration.

Triethanolamine makes an excellent emulsificant; I have used it in the emulsions of oily preparations such as calamine liniment, N. F., or oil of cade in diluted extract of hamamelis water, N. F. The emulsions will stand without separating for a long time.

The following directions have been furnished to me by the Carbide and Carbon Chemical Corporation:

> In making emulsions, dissolve separately fatty acids in oil and triethanolamine in water, and then mix together. Emulsions should first be made in concentra-

tions of from 20 to 40 per cent; if desired they may be diluted later. For emulsions containing olive oil, the properties required are approximately 2 per cent triethanolamine to 15 per cent oleic acid, and are probably the same for the greater number if not all of the vegetable oils. In the case of mineral oils, less fatty acid is required.

Triethanolamine hydrolizes dyes such as gentian violet, brilliant green, crystal violet and fuchsin, producing a colorless solution. On the addition of water the dye is again apparent. I have attempted to determine whether or not this reaction is useful in delivering a dye to the infected area before it is set free by the blood serum, but so far the investigation has lead nowhere.

Finally, I have found a soap made according to the following formula excellent in the treatment for acne; it has also proved to be extremely useful in the removal of stains and dyes from the hands: carbon tetrachloride, 30, triethanolamine, 20, and enough liniment of soft soap, U. S. P., to make 120.

It is naturally impossible for one physician to evaluate correctly a preparation of this sort until a large series of similar cases have been managed in an identical way. However, in order that the field of usefulness for triethanolamine may be increased through its obvious merits, I am presenting this paper in the hope that other dermatologists may extend the work that I have started.

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FUNGUS INFECTIONS OF THE SKIN AND ITS APPENDAGES OCCURRING IN PORTO RICO

A CLINICAL AND MYCOLOGIC STUDY

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Carrión [1] has published detailed mycologic studies together with clinical descriptions and excellent photographs of a number of dermatomycoses occurring in Porto Rico. King [2] and Ashford [3] have also emphasized the frequent occurrence of fungus infections.

In a previous report by one of us (Dr. Kesten)[4] on skin diseases occurring in Porto Rico, it was noted that 42 per cent were clinically typical of fungus infections. Eighty patients (14 per cent) were investigated for the presence of fungi. The object of this paper is to classify the lesions found in these cases according to their distribution and clinical characteristics and to report on the fungi occurring in these clinically similar lesions.

TECHNIC

The affected skin or appendage from which a culture was to be taken was cleansed with soap and water, swabbed with 50 per cent alcohol and allowed to dry. If the lesions consisted of a superficial desquamation or erosion, the

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From the School of Tropical Medicine and the Laboratory for Medical Mycology of the Department of Dermatology, College of Physicians and Surgeons, Columbia University.

1. Carrión, A. L.: Observations on Dermatomycosis in Porto Rico, Arch. Dermat. & Syph. **7**:773 (June) 1923; Preliminary Report on the Fungus Causing Epidermophytosis of the General Surface of the Skin in Porto Rico, Porto Rico J. Pub. Health & Trop. Med. **5**:40, 1929; Observations on Dermatomycosis in Porto Rico, ibid. **5**:278, 1930; **6**:217, 1930.

2. King, W. W.: Some Observations upon the Skin Diseases of Porto Rico, J. Cutan. Dis. **35**:459, 1917.

3. Ashford, B. K.: Significance of Mycology in Tropical Medicine, Arch. Dermat. & Syph. **22**:7 (July) 1930.

4. Kesten, B. M., Observations on Skin Diseases in Porto Rico, Porto Rico J. Pub. Health & Trop. Med. **5**:185, 1929.

epidermis near the edge of the lesion was scraped off with a sterile blunt scalpel. The roofs of vesicles were excised. Portions of affected nails were scraped and small pieces excised from the free border. Broken-off hairs were epilated, and in the deeper infections either a small piece of the affected tissue was excised, or when abscesses occurred they were aspirated, sterile precautions being used. A small portion of the material was placed on a sterile glass slide and a few drops of 10 per cent sodium hydroxide added. After gently warming or allowing the slide to stand for a short time, the disintegrated tissue was examined microscopically for the presence of mycelia and spores. The remainder of the affected material was placed in sterile Petri dishes, and honey agar was then poured over it. If the fungi could not be identified on this medium, they were transplanted to a variety of mediums, including maltose (Sabouraud), dextrose, corn meal or wort agar, and potato or honey broth. In some instances, the fungi were studied from slide or hanging-drop cultures.

OBSERVATIONS

No fungi were obtained in cultures taken from twenty-one of the eighty patients, although clinically they had lesions typical of fungus injections. From the lesions of the remaining fifty-nine patients, from one to four fungi were isolated. The fungi obtained from thirty-two of these patients are known to be pathogenic for the skin. Because of the large number of questionably pathogenic and saprophytic fungi that were also obtained, Petri dishes containing maltose agar (Sabouraud) were exposed in the rooms in which the cultures were taken and identified. The following fungi were recovered: Cephalosporium, Acrothecium, Aspergillus, Penicillium, pink Cryptococcus, Hormodendrum hordei, H. olivaceum and Neurospora sitophila. A report of the lesions grouped according to their distribution together with the fungi found follows:

Fungus Infections of the Scalp (Tinea Capitis).—Cultures were taken from four children with ringworm of the scalp. These children had from one to three rather small indurated areas of almost total alopecia covered with fine scales through which protruded a number of broken-off hairs. Trichophyton gypseum was cultured from the hairs of three of these children, and Trichophyton plicatile from those of the fourth.

Fungus Infections of the Nails (Onychomycosis).—Of the seven patients with a fungus infection of the nails, six had similar infections of the skin. In five of these patients, there was involvement of two or three nails, and in two an accompanying paronychia. The nails involved were usually grayish to grayish black and lusterless, and the free border of the nail plate was thickened and irregular in outline. Cultures taken from four patients showed Monilia, those from one Endodermophyton tropicale and those from another three nonpathogenic fungi, and the culture taken from the remaining patient was sterile.

The two patients with a paronychia as well as an onychia were among those from whom a culture showing Monilia was taken.

Superficial Fungus Infections Leaving Depigmentation (Tinea Flava, Tinea Versicolor, Achromia Parasitaria).—The most superficial fungus infection consisted of numerous minute, whitish areas circumscribing the hair follicles of the exposed glabrous skin. Frequently these small areas coalesced to form an irregular though well defined, nonelevated, slightly adherent squama not greater than 1 cm. in diameter. These lesions occurred on the exposed parts, i. e., the face, neck or arms, of eleven patients with dark skin. There were no symptoms. On direct examination of the squamas, there were numerous nonseptate mycelia, which were frequently T-shaped, and masses of double-ringed spores. Cultures of these squamas showed no pathogenic fungi. In one patient whose skin covering the arms was deep brown and that of the trunk almost white, there occurred the previously described lesions on the arms and the typical yellowish-white, superficial, maculosquamous areas of tinea versicolor on the trunk. On direct examination of the squamas, the fungi from both of these areas were identical with the ones described.

In contrast to these small depigmented lesions, six patients had large, superficial, irregular, smooth, depigmented patches on the exposed surfaces. These also occurred in dark skinned patients, and with the exception of a very slight peripheral desquamation, appeared strikingly like leukoderma. There were no symptoms; the patients usually sought relief because of the disfigurement or for other skin lesions, which were usually due to fungi.

Direct slide examination of the squamas showed numerous elongated mycelia and what appeared to be the same fungus; Hormodendrum was obtained in cultures taken from five patients. On Sabouraud's dextrose agar it produced a raised, grayish-green, buckled growth which in five days attained a diameter of 2 cm. On corn meal agar, the colony reached a size of 1.5 cm. in five days. The growth was flat, velvety and dark olive green, with a lighter margin. The mycelium was septate, branched, hyaline or olive green. The condiophores were erect, simple and olive green, bearing round or oval conidia in short chains. The conidia, also olive green, measured from 3.2 to 5.6 by from 2.4 to 3.5 microns, and were separated by minute hyaline disjunctors as shown in figure 1. This description corresponds with that given by Rabenhorst [5] for Hormodendrum olivaceum (Corda) and that for Hormodendrum fontoynonti (Langeron).[6]

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5. Rabenhorst, L.: Kryptogamen Flora, Fungi imperfecti, Leipzig, Kummer, 1907, vol. 8, p. 702.

6. Brumpt, E.: Précis de parasitologie, Paris, Masson & Cie, 1927, p. 1230.

As Hormodendrum grew on plates exposed in the laboratory and also was one of the fungi found in two other cultures from clinically different lesions, an effort was made to determine its etiologic significance. Cultures that were grown on maltose agar were ground in a sterile mortar, suspended in a small amount of physiologic solution of sodium chloride and then strained through thick gauze. This suspension was rubbed into the previously sandpapered skin of black and

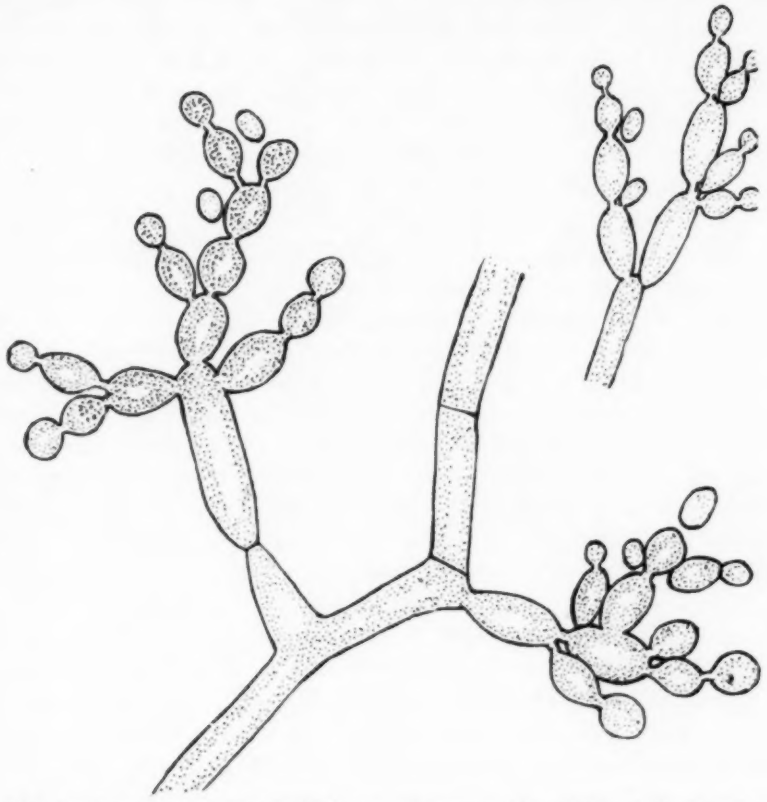

Fig. 1.—Drawing of Hormodendrum olivaceum (?), obtained from patients with achromia parasitaria, showing characteristic conidiophors, with short chains of conidia, which are separated by disjunctors; × 1,100.

of white skinned guinea-pigs and rabbits. No lesions developed following the healing of the initial abrasion. Guinea-pigs and rabbits received small amounts of this suspension intradermally, subcutaneously and intracardially. Discrete nodules, from which Hormodendrum could be recovered, developed at the sites of the cutaneous injections. These animals as well as the ones receiving intracardial injections remained well.

Fungus Infections of the Feet and Hands (Dermatomycosis).—One of the most frequent infections of the skin occurred as whitish sodden and desquamating epidermis between the toes accompanied by small vesicles or vesicopustules along the sides of the toes and the plantar surfaces of the feet. Accompanying the foot infection there occurred frequently either patches of eczema on the leg and hands or minute vesicles along the sides of the fingers or on the palms. These lesions were usually associated with hyperhidrosis. Of the ten patients with dermatophytosis of the feet, seven had lesions on the hands, arms or legs as described. Trichophyton gypseum was obtained on a culture taken from one patient, Epidermophyton inguinale on one taken from another patient, Mycoderma on cultures taken from two patients and Monilia on cultures taken from five patients. In addition, the following saprophytes were obtained: Scopulariopsis trigonospora, Geotrichum candidum, pink Cryptococcus, Penicillium, Aspergillus and Acremoniella.

Superficial Fungus Infections of the Remaining Glabrous Skin.—There were forty-seven patients with other superficial fungus infections of the glabrous skin, in three of whom the lesions were disseminated; in thirty they were predominant on the extremities, in four they were confined to the trunk, and in nineteen they were present on the face and neck. As noted previously by Carrión,[1] there was almost no area of the skin that was not involved, and a few patients exhibited a variety of lesions. The majority of lesions were sharply circumscribed, but occasionally they were dffuse. Most commonly there occurred a superficial patch of erythema with an irregular, slightly infiltrated border. The patches were covered with vesicles, papules, squamas or a combination of these lesions. Occasionally there was a central area of denuded epidermis with an irregular undermined edge. Frequently the patch varied in color from the surrounding skin. More rarely, the lesions involved the dermis and were surmounted with the same type of lesions as the superficial patches. Occasionally these lesions were accompanied by fungus infections of the appendages. The occasional disseminated eruptions were usually macular or papular and from red to purple, and they accompanied the patches just described. Cultures taken from the epidermal scrapings of thirteen of these patients showed no fungus growth. From the remaining thirty-four patients of this group, sixty-five fungi were obtained. Cultures taken from seven contained fungi usually accepted as pathogenic for the skin, namely, Endodermophyton tropicale (three), Microsporum lanosum (two) and Trichophyton gypseum (two). Cultures taken from ten other patients were of questionable pathogenicity and included: Hormodendrum olivaceum (?) (two), Monilia (seven) and Mycoderma (one). The remaining fungi that were isolated are usually

regarded as saprophytic. They were: pink Cryptococcus, black Torula, Oidium, Haplographium, Cephalosporium, Chaetomium, Acrothecium, Acremoniella, Alternaria, Aspergillus, Penicillium, Scopulariopsis, Phoma, Fusarium, Dematium and Mucor.

Deep Fungus Infections of the Skin.—Of the four deep fungus infections studied, two were strikingly similar. On the flexor surface of the forearm of each patient there was a large flattened tumor with irregular borders. The surface of the tumors was reddened and glossy, and contained numerous small fistulas. On pressure or when the orifices of these fistulas were probed, a horny plug was extruded, and then followed a profuse, thin, yellow discharge. The lesions were

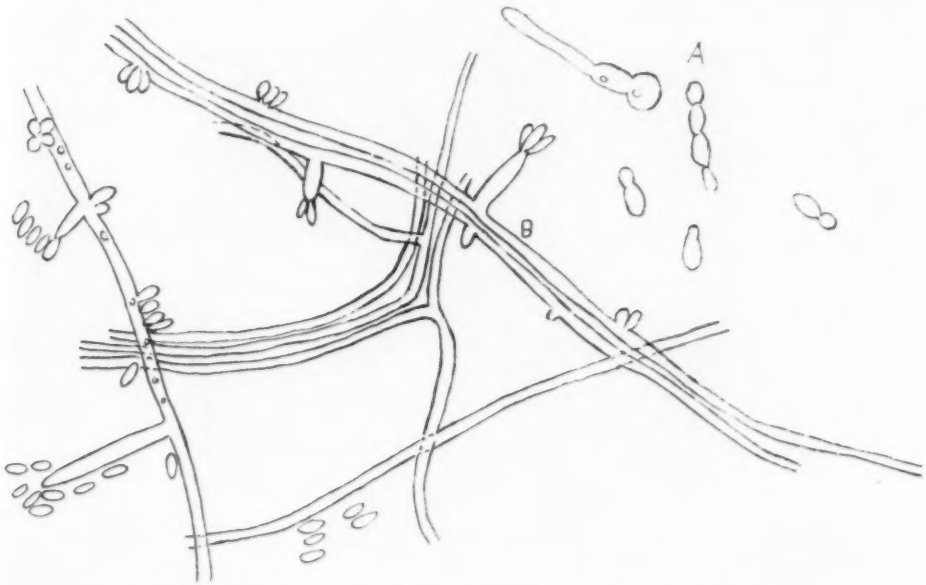

Fig. 2.—Drawing of Sporotrichum gougeroti, showing (*A*) budding cells, (*B*) characteristic mycelium and spores. The spores are sessile or are on short lateral branches; × 700.

moderately firm and slightly tender. There was a slight epitrochlear adenopathy. The possibility of actinomycosis was considered clinically. However, no actinomycetes were found on direct examination of the pus or on cultures of the pus or on those taken from a piece of excised tissue. Hemolytic staphylococci were obtained from the lesion of one patient, and a brown yeast and Monilia from that of another. No definitely pathogenic fungus was found. Biopsy of a specimen taken from one of the lesions showed only a chronic inflammation. Both patients were given iodides, and the one who was observed for two months showed an almost complete regression of the lesion.

The third patient had multiple lesions on the genitalia. Two weeks previous to examination the patient had noted a small ulceration on the penis. On examination, there were four small rather superficial ulcerations on the dorsum of the penis. These had a granulomatous base and exuded a grayish-yellow, thick, odorless pus. Also along the dorsum of the penis, over the pubes and extending to the inguinal glands were nodular swellings from 1 to 3 cm. in diameter. They were acutely inflammatory, fluctuating and tender. Pus aspirated under sterile precautions from one of the closed gummatous lesions was planted on Sabouraud's agar. A fungus developed which formed round raised colonies with a black velvety surface, rather friable in consistency. Microscopically, it was seen to form a coarse septate mycelium

Fig. 3.—The superficial ulcerating lesion on the toes from which Penicillium spiculisporum was cultivated.

containing considerable black pigment with numerous oval spores from 1.5 to 2.5 by from 3.5 to 5.5 microns in diameter. The spores were usually at the end of short undifferentiated side branches, but were frequently sessile (figure 2). Numerous free conidia were found in the culture, some of which developed distinct buds. The organism appeared identical with a stock culture of Sporotrichum gougeroti obtained from Dr. Sabouraud. The patient's Wassermann reaction was positive, and the lesions cleared entirely on antisyphilitic therapy, which included potassium iodide.

Cultures of the patient's Sporotrichum were suspended in saline, as previously described, and injected into the heart, testicle and skin of rats and into the heart and skin of a monkey. The rats that received the injections into the testicle developed a moderate swelling and a few

small yellowish abscesses in the testicle. Sporotrichum gougeroti was recovered from these abscesses. The other animals remained well.

This species of Sporotrichum, which was first found by Gougerot in a deep abscess, has since been reported in various types of chronic inflammatory lesions. Grütz was able to collect ten cases from the literature, including one of his own. In many of the cases there was frank suppuration as in the case reported here. Several of the patients presented large solitary abscesses or extensive ulcerations. Only one showed a typical arrangement of gummas along the course of the superficial lymphatics, which is so frequently found in infections with Sporotrichum schenckii. In the present case, the gummatous lesions seemed

Fig. 4.—Penicillium spiculisporum Lehman. The colony has been for three weeks on Sabouraud's maltose agar, and shows many ascocarps.

to develop along the course of the lymphatics draining the penis. Suppuration was marked. The small ulcers on the distal portion of the penis resembled the papulo-ulcerative lesions described by Grütz.

The fourth patient had rather symmetrically distributed, superficial, ulcerating lesions on the lower extremities. Pustules first appeared on the plantar surface of the great toes, and as these became ulcerated (as shown in figure 3) new lesions appeared on the lateral sides of the feet and on the extensor and lateral surfaces of the legs and thighs. The patient had about twenty ulcerations, the size depending on the age of the lesion. On the toes the ulcerations were about 1.5 cm. in diameter and had a well rounded, infiltrated border; the base was

rather superficial and was covered with a yellow blood-tinged exudate. An erythematous area of about 0.5 cm. surrounded each lesion. The lesions were distinctly tender on pressure. The other ulcerations were similar but less advanced.

Cultures taken from these open ulcers gave a pure growth of a fungus of unusual character. On Sabouraud's maltose agar, the

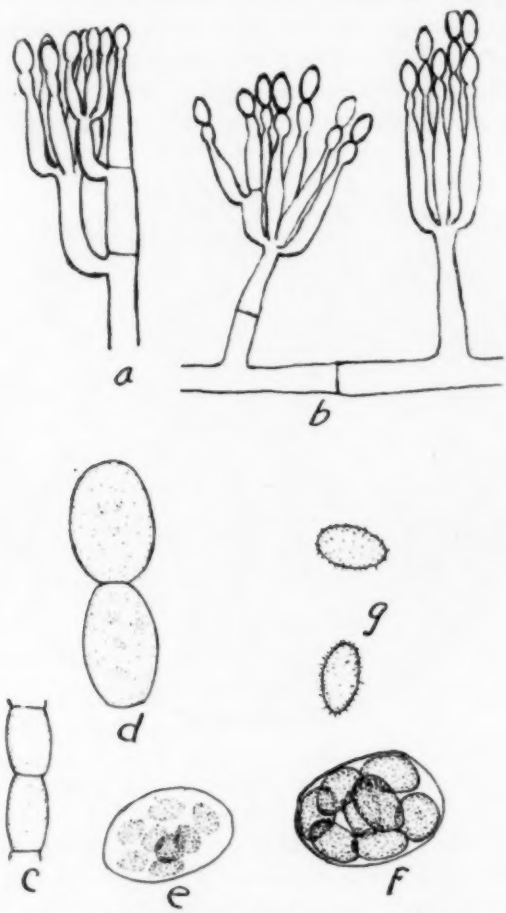

Fig. 5.—Drawing of Penicillium spiculisporum Lehman; *a*, indicates an asymmetric type of conidiophore; *b*, typical conidiophores; *c*, a young ascogenous hypha; *d*, ascogenous hyphae; *e*, a young ascus, containing immature spores; *f*, a mature ascus with spores; *g*, mature ascospores; × 1,100.

colonies developed rapidly. They were at first white and downy, and later cream colored and granular. The surface was radially grooved. On Czapek's agar, growth was slower and the color more intense, becoming greenish yellow with age. The hyphae were from 2 to 3.5

microns in diameter, and the conidiophores were from 2.5 to 2.7 by from 8 to 20 microns. Usually each conidiophore bore a single verticil of sterigmas. Occasionally the sterigmas were biverticillate and asymmetric. There were usually from three to several long, tapering, delicate sterigmas in a verticil. The conidia measured from 2 to 3 by from 2.5 to 5.5 microns. They were round, oval or occasionally slightly pointed at the distal end. The granular appearance of the older cultures was due to the presence of numerous ascocarps. The ascocarps were subglobose, from 0.3 to 3 mm. in diameter and yellowish, with a tough wall of fine hyphae. The asci were elliptic to globose and measured from 6 to 7.5 by from 7 to 10 microns, and were usually eight-spored. The ascospores measured from 1.8 to 3 by from 2.5 to 4 microns, were elliptic and were covered with minute spines. The characteristics are shown in figures 4 and 5. Dr. Charles Thom identified this fungus as Penicillium spiculisporum. This species was first isolated by Lehman from the rootlets of cotton plants and was later found in soil.

A saline suspension of this Penicillium was injected intracutaneously, subcutaneously, intratesticularly and intravenously, as well as rubbed into the scarified skin of rabbits and rats. A monkey also received subcutaneous and intracardial injections of the suspension. All of the animals developed inflammatory nodules at the sites of intracutaneous and subcutaneous injections. The nodules gradually reabsorbed without ulceration. In the rat, following the intratesticular inoculation, the testicle became markedly swollen. At autopsy a month later, all of the organs were normal except the testicle, which was hemorrhagic and atrophic but without abscesses. Penicillium spiculisporum was again obtained in a culture taken from this testicle as well as in cultures taken from the nodules that followed injections into the skin.

In this case the fact that the fungus was isolated from open lesions and failed to reproduce characteristic lesions in animals leaves its etiologic significance in some doubt. It was obtained, however, from several of this patient's lesions in pure culture and was never observed in the numerous other lesions investigated, nor in cultures from the dust of the rooms in which this work was carried on.

COMMENT

The number and variety of skin lesions that may be caused by fungi are attracting increasing interest. However, in many cases in which a clinical diagnosis of fungus infection is made, no fungi can be demonstrated. In many other lesions in which fungi are present, proof is lacking that they are the cause of the skin infection.

In the present report, fungi were cultivated from 73 per cent of the patients, but fungi known to be pathogenic to the epidermal

structures were cultured from only 46 per cent of the lesions. Their frequency of occurrence was in the following order: Monilia, Trichophyton, Hormodendrum, Endodermophyton, Microsporum, Epidermophyton and Sporotrichum. With the exception of the Sporotrichum and Hormodendrum, the fungi mentioned produced no clinically distinctive lesions, so that in general one is unable to associate any particular fungus with a particular type of superficial fungus infection of the skin. Also, the same species of fungus is found in clinically dissimilar lesions.

Pathogenic fungi were obtained in cultures taken from the majority of the infections of the scalp and nails. The inability to cultivate the fungus (Microsporum furfur?) seen on direct slide examination of the squamas from eleven patients with tinea flava might make its significance doubtful were it not for its unique and almost constant occurrence in this type of lesion. Castellani [7] has pointed out the morphologic similarity, if not identity, of the organism found in tinea flava and tinea versicolor. The presence of these two clinically different lesions on the exposed and unexposed skin of the same patient suggests that tinea flava and tinea versicolor are due to the same fungus, and that the difference in the color of the lesions is related to the effect of light and the fungus on the skin.

Pardo-Castello and Dominguez [8] isolated a fungus "which might be classified among the Aspergillaceae" from 16 per cent of their thirty-six cases of achromia parasitaria. They were unable to reproduce the lesions experimentally in animals. However, Brumpt [6] described achromie parasitaire due to Hormodendrum fontoynonti, and he stated that lesions have been reproduced experimentally in man. The species here called Hormodendrum olivaceum is apparently the same as that described by Brumpt. The fact that it was found on culture plates exposed in the laboratory and in two cultures from clinically different lesions throws some doubt on its etiologic importance. Nevertheless, and in spite of the inability to reproduce the lesions in animals, it seems probable that the presence of Hormodendrum in five of the six patients with the areas of leukoderma is of etiologic significance.

The presence of Sporotrichum gougeroti and Penicillium spiculisporum in pure cultures from the pus of a patient with deep fungus infections and the recovery of these organisms from the lesions of inoculated animals seem of etiologic importance, although the disease was not reproduced experimentally. Fungi belonging to Penicillium

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7. Castellani, A.: Fungi and Fungous Diseases, Chicago, American Medical Association, 1928, pp. 158 and 190.

8. Pardo-Castello, V., and Dominguez, M. M.: Achromia Parasitaria, Arch. Dermat. & Syph. **9**:82 (Jan.) 1924.

group (Mastigocladium and Scopulariopsis) have been isolated in cladiosis [9] from gummatous lesions similar to those found in sporotrichosis. These fungi were also found to be only slightly pathogenic for animals. However, the lesions from which Penicillium spiculosporum was obtained on culture did not simulate sporotrichosis, but rather the description given by Castellani [7] for the ecthymatous type of accladiosis that is due to an entirely unrelated fungus, Acladium castellanii Pinoy.

Eighteen fungi usually regarded as saprophytes were recovered from making the cultures, as six of the same species developed on plates exposed to the air of the clinic and laboratory. On the other hand, some may have been growing saprophytically on the skin and still others may be pathogenic for the skin, though experimental evidence of their pathogenicity is lacking.

SUMMARY

Fungi thought to be pathogenic to epidermal structures were found in cultures taken from the lesions of 46 per cent of eighty patients with infections of the skin and appendages clinically resembling mycoses.

With the exception of achromia parasitaria, the pathogenic fungi and the superficial skin lesions produced by them were essentially the same as those found in the more temperate climates.

A case clinically similar to the ecthymatous type of accladiosis (Castellani), but from which Penicillium spiculisporum was isolated, is reported.

Dr. W. Galbreath, Dr. J. Suárez and the Staff of the Presbyterian Hospital, Dr. G. B. Dowling and Dr. P. Morales-Otero gave us the opportunity of studying these patients.

9. Bloch, B., and Vischer, A.: Die Kladiose, Arch. f. Dermat. u. Syph. **108**: 476, 1911. Matruchot, L.: Un nouveau champignon pathogène pour l'homme, Compt. rend. Acad. d. sc. **152**:325, 1911. Grütz, O.: Dermatomykosen, in Jadassohn, J.: Handbuch der Haut und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 9, p. 800.

SELF-STERILIZATION POWERS OF THE SKIN

II. THE BODY FOLDS

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In the introductory paper [1] of this series, experiments were reported to show that the skin has the capacity of inactivating micro-organisms on its intact surface. The rate of this inactivation was determined on various parts of the intact skin, over the lesions of some pathologic conditions and before and after the use of some standard forms of therapy. Some of the results that were reported indicated that moisture may partially inhibit the sterilizing process. There was some speculation as to what rôle the air might play in this. Since the body folds are moist and to a degree exclude air currents, they were selected for the next set of studies, which are reported here.

METHOD

The method for determining the sterilization rate of the skin was the same as that which was used in the first study of this series. An emulsion of the trial organism, Staphylococcus aureus, was made, as described previously, and spread evenly on the area to be tested. Immediately after this, a swab previously moistened with distilled water was passed over one half of the seeded surface, and the other half was similarly swabbed at the end of a half hour test period. The material that clung to the swab was plated on Petri dishes. The number of colonies on the plates for each half area indicated in a manner the rate at which the tested organisms were arrested in their activity. One variation in technic was thus made. Only two swabbings were made, one at the beginning and the other at the end of the thirty minute period, instead of the customary four during the same interval. Observations were thus reduced to the minimum, in order to keep the condition of the parts as nearly natural as possible.

The results are summarized in the accompanying table.

CONCLUSIONS

1. Skin folds are less able to inactivate micro-organisms than are other normal cutaneous areas.

Submitted for publication, June 11, 1931.

From the Department of Dermatology, University of Illinois College of Medicine, Service of Dr. F. E. Senear.

1. Cornbleet, T., and Montgomery, B. E.: Self-Sterilization Powers of the Skin, Arch. Dermat. & Syph. **23**:908 (May) 1931.

2. Their self-sterilizing capacity is still further depressed whenever they become the seat of a pathologic disturbance.

3. When skin folds are opened to the air, their capacity to inactivate staphylococci tends to approximate that of other normal skin areas.

Percentage of Organisms Remaining Active at End of Test Period *

1. Inframammary Fold:	
a. Breast held aloft, area seeded immediately on raising breast, and organisms removed at end of thirty minutes	20
b. Breast held aloft, area seeded thirty minutes after raising breast, and organisms removed thirty minutes later	12
c. Breast down, organisms removed thirty minutes after seeding test area	84
d. Breast down, organisms removed one hour after seeding test area	80
2. Axilla:	
a. Arm up (observation similar to 1 *a*)	32
b. Arm up (observation similar to 1 *b*)	22
c. Arm down (observation similar to 1 *c*)	61
d. Arm down (observation similar to 1 *d*)	57
3. Interdigital Spaces of Toes:	
A. Gross appearance normal	
a. Toes apart (observations similar to 1 *a*)	24
b. Toes apart (observations similar to 1 *b*)	15
c. Toes approximated (observations similar to 1 *c*)	73
d. Toes approximated (observations similar to 1 *d*)	70
B. Eczematoid ringworm dermatitis present clinically	
a. Toes apart (as 3 *A*, *a*)	83
b. Toes apart (as 3 *A*, *b*)	75
c. Toes approximated (as 3 *A*, *c*)	88
d. Toes approximated (as 3 *A*, *d*)	87
4. Perianal Fold:	
A. Gross appearance, normal	
a. Open (observation as in 1 *a*)	28
b. Open (observation as in 1 *b*)	19
c. Closed (observation as in 1 *c*)	76
d. Closed (observation as in 1 *d*)	74
B. Gross appearance pathologic, hemorrhoids, etc.	
a. Open (as 4 *A*, *a*)	89
b. Open (as 4 *A*, *b*)	85
c. Closed (as 4 *A*, *c*)	96
d. Closed (as 4 *A*, *d*)	96
5. Palms, Normal Appearance:	
a. Not clasped, organisms removed thirty minutes after seeding	6
b. Clasped, bandage around hands, organisms removed thirty minutes after seeding	53
c. Clasped, organisms removed one hour after seeding	50

* Average values of the results obtained in the number of trials in each category.

4. This tendency is a function of time; the longer the fold remains open, the closer is the approximation.

5. The total number of organisms inactivated in a closed skin fold bears little relation to time.

FOLLICULITIS ULERYTHEMATOSA RETICULATA

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I felt justified in publishing a detailed description of this case because of the apparent paucity in the literature of reports of cases of this type.

REPORT OF A CASE

History.—R. M., a school girl, aged 15, was referred to the clinic because of an eruption on her face. She stated that the eruption had been present for the past five years, beginning as a slight roughness and redness and progressing to the condition for which she sought consultation. At no time did the patient notice the appearance of papules, pustules or vesicles. She said there had been no injury. The family history was negative for any skin disease. The personal history was unimportant.

Examination.—Symmetrically arranged on both cheeks, the outer portions of the eyebrows and the glabella were numerous closely crowded small areas of atrophy separated by narrow ridges which produced a reticulated, honey-combed or network appearance. Each atrophic area presented an abrupt pitlike depression varying in size from that of a pinpoint to that of a small split pea. The pitlike appearance was less prominent in some of the atrophic areas, which resembled the scarring of the superficial type of varicella. Among the ridges a few small comedones were noted; milium-like lesions were absent at the patient's first visit, but subsequently developed. The skin covering the ridges was even with the normal skin and was contrasted with it by a waxy, firmer and somewhat stretched appearance. On close inspection through a magnifying glass a definite redness was apparent, which was due to a small, fine capillary ramification. About the nasolabial folds the skin appeared greasy, and small comedones were present. The medical examination otherwise gave essentially negative results.

Pathologic Report.—Histologic slides were studied by Dr. George M. MacKee of New York City, to whom I am indebted for the following report:

Examination of the serial sections revealed no significant changes in the epidermis. It was somewhat thin and slightly hyperkeratotic, and there were very few rete pegs. In the derma, the capillaries were dilated and the walls were edematous. There was a moderate round cell infiltration, which was mostly perivascular. There was slight edema of the collagen with some fragmentation and beginning of basophilic degeneration in places. The most interesting changes were in relation to the appendages. Several large, tortuous, dilated hyperkeratotic follicles were present. There were many large cavities lined with epithelial cells; most of these cavities had thin walls that contained keratin, while others were empty. These were horn cysts mostly caused by tangential sections of the follicles. Some showed no apparent derivation, while others were connected with follicles by thin epithelial bridges. There was one so-called double comedone; in other words, a union of two markedly hyperkeratotic follicles. Very few sebaceous glands were present.

Submitted for publication, Aug. 28, 1931.
From the Dispensary Service of Allegheny General Hospital.

Fig. 1.—Photograph of patient with folliculitis ulerythematosa reticulata.

Fig. 2.—Photomicrograph of section (low power).

The pathologic diagnosis was folliculitis ulerythematosa reticulata, possibly an early case in a young subject.

Treatment.—All methods of treatment except roentgen therapy were instituted, and proved of no avail.

COMMENT

Darier [1] stated that the first mention of this disease was made by Thibierge [2] in 1900 under the title of "vermicular acne," a name proposed by Besnier. Furthermore, he stated that the disease is one occurring in childhood, attacking both cheeks symmetrically and giving the skin a distinct appearance of worm-eaten wood; the etiology is unknown, the course is chronic and the duration is indefinite.

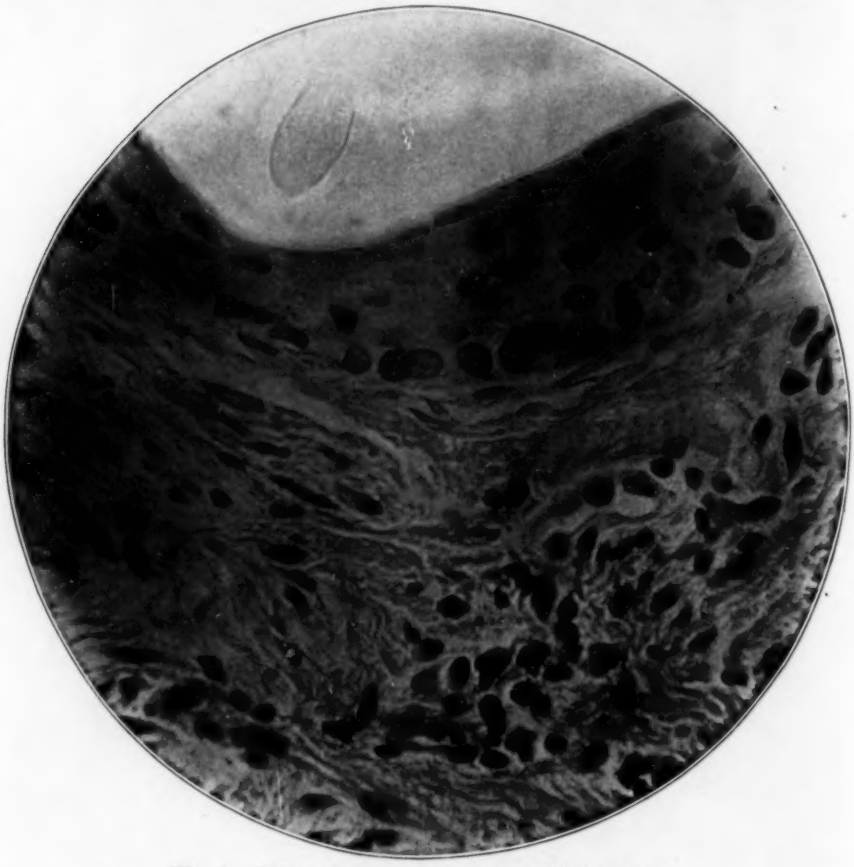

Fig. 3.—Photomicrograph of section (high power).

The case here described was almost identical with that reported by MacKee and Parounagian.[3]

1. Darier, J.: Bull. Soc. franç. de dermat. et syph. **27**:345, 1920.
2. Thibierge: Acne, in La pratique dermatologique, Paris, Masson & Cie, 1904.
3. MacKee, G. M., and Parounagian, M. B.: J. Cutan. Dis. **36**:339, 1918.

A SIMPLE METHOD OF TREATING MUCOUS RETENTION CYSTS OF THE LIP

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NEW YORK

Numerous ways of dealing with mucous retention cysts have been described. Sutton,[1] in an article on the subject, stated that in his experience removal of the sac in toto gave the best results. Pusey, in the discussion of Sutton's paper, said that opening of the cyst, followed by cauterization with iodine, phenol or silver nitrate, was invariably followed by recurrence. His treatment consists of incising the cyst and thoroughly cauterizing the cavity with a small point cautery. This produces a cavity that looks quite formidable but that heals with practically no scarring. Da Costa, in his latest edition of "Modern Surgery," [2] outlined the treatment as follows: incision, curettement and cauterization by pure phenol and packing, or extirpation of a considerable part of the cyst and cauterization of the remaining part. Others attempt to destroy the cyst lining by electrocoagulation through an opening in the wall.

The foregoing methods of treatment fall principally into two classes: in one, the cyst is completely extirpated and the resulting wound sutured; in the other, the cyst is left in place, and an attempt is made to destroy its lining by some form of cauterization. The former method gives perfect results when thoroughly done. It is, however, by no means an easy operation because of the friable nature of the cyst wall and the inevitable profuse bleeding accompanying the procedure. With the second method, some workers, notably Pusey, have secured satisfactory results using the direct cautery; with other methods of cauterization, a recurrence is likely.

I have been using a method radically different from those that have been described. It is both simple and efficient and can be performed in a physician's office in a few minutes.

Submitted for publication, Aug. 27, 1931.

From the services of Drs. Charles Mallory Williams, Paul E. Bechet and Eugene F. Traub at the Stuyvesant Square Hospital, formerly the New York Skin and Cancer Hospital.

1. Sutton, R. L.: Retention Cysts of the Mucous Membrane of the Lip, J. Cutan. Dis. **36**:579, 1918.

2. Da Costa, V. C.: Modern Surgery, ed. 10, Philadelphia, W. B. Saunders Company, 1931, p. 315.

Figure 1 represents schematically a vertical cross-section of a mucous cyst and the overlying mucosa. With the cutting current of an endothermy apparatus, preferably, or with a scalpel, the incision *AC* is made, through the oral mucosa and into the cyst cavity at one end. The cutting instrument is passed around the entire margin of the cyst cavity, thus removing a more or less circular mass of tissue, consisting of the roof of the cyst, made up of the oral mucosa, *AB*, and the portion of cyst membrane, *CED*. Figure 2 shows the portion that remains after the operation is completed, with the floor, *CFD*, of the cyst still present. No attempt is made to cauterize the latter. In fact, cauterization is contraindicated in this procedure, as it would substitute a raw surface for one

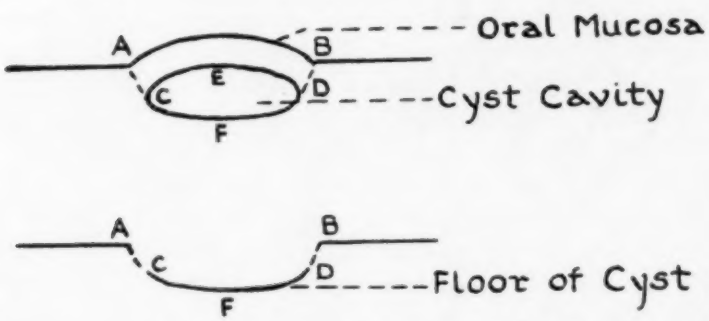

Diagram representing cross-section of a mucous cyst (upper figure) before and (lower figure) after operation.

already covered with epithelium. No suturing is necessary, and healing is extremely rapid. Recurrence does not take place, because any mucus secreted by the floor of the cyst is not retained in a closed cavity but passes directly into the mouth. In time the character of the cyst floor changes to that of normal oral mucosa.

I have used the same procedure in the treatment of a hydrocystoma, 0.5 cm. in diameter, situated near the outer canthus of the left eye. By merely removing the roof of the cyst, including the overlying skin, a complete disappearance of the lesion was obtained; within a few weeks no difference could be observed between the character of the cyst floor and that of the surrounding skin.

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BISMARSEN IN THE TREATMENT FOR CONGENITAL SYPHILIS

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AND
GEORGE F. KOETTER, M.D.
LOS ANGELES

Simplification in the treatment for syphilis, especially congenital syphilis, is indeed desirable, provided therapeutic effectiveness is equal to modern standards of therapy.

Bismarsen is a drug that appears to meet these requirements. Simplification is apparent in the intramuscular administration of a medicament combining soluble bismuth and an arsphenamine derivative in a single dose, and therapeutic effectiveness is apparent in the following data which represent a two and one-half years' clinical observation of the drug in the treatment for congenital syphilis.

Bismarsen or bismuth arsphenamine sulphonate was discovered by Raiziss and has the empiric formula of $C_{21}\ H_{21}\ O_{12}\ As_3\ Na_3\ S_3\ N_3\ Bi_2$.

Clinical observation in the use of bismarsen was first reported by Stokes and Chambers [1] in 1927, later by O'Leary [2] in 1928, Tobias [3] in 1928, Elliot [4] in 1929, Kolmer [5] in 1929, Templeton [6] in 1929, Shivers [7] in 1930 and Stokes, Miller and Beerman [8] in 1930. All of these writers

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Submitted for publication, July 24, 1931.

From the Department of Dermatology and Syphilology, Children's Hospital, Los Angeles.

1. Stokes, J. H., and Chambers, S. O.: Bismuth Arsphenamine Sulphonate: Clinical Observations on New Arsphenamine Synthetic in Treatment of Syphilis, J. A. M. A. **89**:1500 (Oct. 29) 1927.

2. O'Leary, P. A.: Bismuth Arsphenamine Sulphonate: New Synthetic Drug for Intramuscular Use in Treatment of Syphilis, Arch. Dermat. & Syph. **18**:372 (Sept.) 1928.

3. Tobias, N.: Am. J. Syph. **12**:536 (Oct.) 1928.

4. Elliot, J. A.: Southwestern Med. **22**:785 (Sept.) 1929.

5. Kolmer, J. A.: Bismuth Arsphenamine Sulphonate in the Treatment of Syphilis and of Other Spirochetic Infections, Arch. Dermat. & Syph. **21**:394 (March) 1930.

6. Templeton, H. J.: California & West. Med. **30**:55 (Jan.) 1929.

7. Shivers, C. H.: Clinical Value of Bismarsen in Treatment for Syphilis, Arch. Dermat. & Syph. **22**:462 (Sept.) 1930.

8. Stokes, J. H.; Miller, T. H., and Beerman, H.: Appraisal of Newest Arsphenamine Synthetic Bismarsen in Treatment for Syphilis, Based on 7,666 Injections in 341 Cases During Five Years, Arch. Dermat. & Syph. **23**:624 (April) 1931.

included in their reports a few examples of congenital syphilis treated with bismarsen, insufficient, however, to permit conclusions.

Bismarsen was placed in the department of dermatology and syphilology of the Children's Hospital in September, 1928, as the sole agent in the treatment of its syphilitic patients.

A group of 180 children and infants have been observed for periods varying from one and one-half years to two and one-half years. A total of 6,349 injections have been given to date. Serologic effects were studied through the cooperation of the main laboratory under the direction of Dr. C. M. Hylan. The Kolmer and Kahn technics were employed in this procedure.

The subjects varied in age from birth to 14 years, the majority being more than 3 years of age.

Dosage Used at Children's Hospital

Age	Dosage (Dissolved in 2 Cc. Solvent)	
2 weeks	10 to 20 mg.	0.1 to 0.2 cc.
2 to 6 weeks	20 to 30 mg.	0.2 to 0.3 cc.
6 to 12 weeks	40 to 50 mg.	0.4 to 0.5 cc.
3 to 12 months	75 mg.	0.75 cc.
	Dissolved in 1 Cc. Solvent	
1 to 2 years	100 mg.	0.5 cc.
2 to 3 years	100 mg.	0.5 cc.
3 to 4 years	100 to 150 mg.	0.5 to 0.75 cc.
4 to 5 years	150 to 200 mg.	0.75 to 1 cc.
5 to 14 years	200 mg.	1 cc.

TECHNIC AND FREQUENCY OF ADMINISTRATION

The drug was administered according to the dosage shown in the table.

The technic of injection, while basically epifascial, resolved itself into placing the medicament in positions in the buttocks where injections had not recently been given. We felt relatively certain that repeated injection in the same site or near it resulted in greater local reaction. Infiltrated areas were avoided on subsequent injections, hence confinement to the inner angle of the upper and outer quadrant was not possible, and according to our experience is not advised in the use of bismarsen where frequent injections are necessary. The use of deep pressure in massage is advisable. A heavy pestle-like instrument is placed over the site of injection and rotating pressure exerted for ten minutes. The patient is instructed to massage the buttock similarly ten minutes each night for three nights following the injection.

The dose is best given twice weekly, twenty injections to the course with rest intervals of two weeks between courses one and two and one

month between courses two and three. A total of three courses are advised, although five children of our series received as many as five courses without discomfort or evidence of toxicity.

RESULTS OF ADMINISTRATION

Effect on the Patient.—The local reaction equals that to other of the intramuscular arsphenamine derivatives, oil suspensions of bismuth and water-soluble bismuth preparations. Without strict observance of technic and filtration through gauze, the reaction rises in degree. Previous to filtration methods, it was necessary to discontinue treatment in 5 per cent of our series. Since the latter method has been utilized along with technical care and massage, not a single patient has been withdrawn from treatment. It is interesting to note that removal by filtration of glass particles which would otherwise be injected is apparently not the reason for the avoidance of local reaction by this method, as shown by one of us.[9]

Three patients had nitritoid reactions following injection, which were readily controlled with epinephrine, and subsequent reactions were prevented by the Besredka technic of divided dosage.

Therapeutic Shock.—The Herxheimer effect was noted in but a single secondary eruption. One iritis was apparently intensified following a first injection of bismarsen. No other untoward effects were observed in this respect.

Healing Effect.—Our original experience with the drug was here again recalled, for secondary cutaneous lesions required from ten to fourteen days to clear, bismarsen here lagging slightly behind other of the arsphenamine derivatives.

Interstitial keratitis, of which we had twenty examples, responded favorably.

Clinical classification was based on the degrees of infiltration and vascularization. Twelve of the eyes graded I to II underwent gradual progressive improvement to apparent cessation of pathologic activity in from six to eight weeks. Eight of the eyes graded II to IV cleared in from twelve to sixteen weeks. Granted a slowness of action of the drug in this respect, as noted by Stokes and his co-workers and Kolmer, it is likewise of interest that the residual damage as judged by visual impairment is no greater than that reported in the use of arsphenamine and mercury. The slow consistent healing effects of bismarsen in contrast to the too rapid healing effects of arsphenamine might in part explain this favorable effect. Fifty per cent of the eyes retained a

9. Chambers, S. O.: J. Lab. & Clin. Med. **16**:282 (Dec.) 1930.

vision of 20/30 or better. Vision was 20/60 or better in 70 per cent of the eyes, while 30 per cent retained a vision of 20/70 or worse. One eye retained only light perception.

Photophobia, a constant complaint in all twenty eyes, diminished in intensity until complete disappearance in from fourteen to twenty-one days.

Periostitis and similar conditions respond with marked rapidity, the response being equal to that obtained with other methods of medication.

Toxicity.—After 6,349 injections evidence of toxic effects has been entirely lacking. No reactions suggesting aleukemia hemorrhagica were observed. In two cases bismuth stomatitis resulted from the use of the drug and the cause was verified by the clearing after cessation of treatment and recurrence when the drug was again administered. Five cases showed bismuth lines during the course of treatment. No evidence of jaundice or renal irritation was observed. Urinalyses were made as a routine measure every two weeks.

There was no clinical evidence of unfavorable effect on the organs of special sense so far as we were able to determine.

Effect on the Wassermann Reaction of the Blood.—Two blood samples were drawn before each course of treatment, after the tenth injection and at the end of each course.

In comparing dosage groups, i. e., those receiving two injections weekly and those receiving but one, it was at once apparent that the Wassermann reversal was roughly proportional to the frequency of administration.

Of our total biweekly series, one hundred patients received sixty injections over a period of thirty-six weeks. In 31 per cent of this group the reaction became negative the tenth week; in 40, after the twentieth week and in 20, after the fortieth week. Of this same series one hundred received three full courses of treatment. Sixty-five per cent of this group had complete Wassermann reversal. This represents an excellent serologic effect. In 35 per cent the reaction remained positive, 10 per cent being of the Wassermann-fast group before treatment was started.

Effect on the Fixed Positive Wassermann Reaction of the Blood.—We accepted as treatment standard for this group patients who had received three separate courses of intramuscular sulpharsphenamine, each course comprising from eight to twelve injections, and a similar number of courses of mercury inunctions, each course comprising thirty rubs. The Wassermann reaction of the blood in this group must have remained positive (total to 75 per cent inhibition) at the beginning of treatment, after each course and at the conclusion of treatment, for inclusion in the Wassermann-fast group. Forty-two patients are reported in this group having completed three courses of treatment.

Complete serologic reversal occurred in 51 per cent; 8 per cent showed signs of ultimate reversal, while in 41 per cent the reaction was unchanged. Wassermann reversal occurred by the tenth week in 4 per cent, by the twentieth week in 25 per cent and by the fortieth week in 71 per cent. This again is a truly remarkable record if sustained.

Serologic Relapse.—Of the total group who completed three courses of treatment and were then placed on observation (monthly examination and serologic check), forty-one have been observed twenty months, thirty sixteen months, and twenty-nine twelve months. Of the forty-one patients under observation twenty months following their last treatment, 3 per cent had serologic relapse; of those observed for sixteen months, 2 per cent, and, of those observed for twelve months, 2 per cent.

Effect on the Spinal Fluid.—As a routine procedure, all patients were subjected to the spinal puncture before treatment was instituted and again at the completion of the third course. In but two of the total group were abnormal fluids encountered. A recheck of the spinal fluid following the three courses of treatment showed the normal fluids unaltered. The abnormal fluids likewise remained unchanged.

Clinical Forms of Relapse.—Of the twenty patients with interstitial keratitis completing three courses of treatment, eight have been subsequently observed for eighteen months and twelve for eight months. Relapse that occurred during treatment was observed in but two of the twenty patients. Two patients developed interstitial keratitis during their first ten injections of bismarsen, but the condition cleared on continuance of treatment without signs of relapse twelve months after cessation of therapy.

We did not witness relapse in any other clinical form.

Stimulant or Depressant Effect.—The tonic properties of bismarsen here again were evident, as weight gains checked weekly surpassed those of a similar normal group of outpatient children. Average weights, however, for the syphilitic group before treatment was instituted appeared considerably less than those for the comparative group. Such a consistent weight gain was a welcome effect and at times stimulated cooperation when we might otherwise have failed.

SUMMARY

Apparent therapeutic effectiveness combined with the qualities of simplicity of administration and lack of toxicity should place bismarsen among the antisyphilitic remedies of choice in the treatment for congenital syphilis. Children undergo bismarsen therapy with little or no complaint, which is in vivid contrast to intravenous therapy in this same group. Certainty of dosage in comparison with older mercurial inunction methods is indeed an added advantage. Local reaction is diminished

to the level of comfort, provided the methods of filtration and injection described are utilized, and does not represent an objection to its use. Relapse, clinical or serologic, cannot be determined in so short a period of observation. It is our intention to continue observation and treatment of this same group for years to come. The effect of the drug on interstitial keratitis is extremely satisfying, which is certainly an important consideration. Dosage limitations would appear to be correctly established.

Two injections a week are advised in courses of twenty with rest intervals of two weeks and a total of three courses. The serologic record is gratifying indeed, and the lack of toxicity emphasizes safety in general hands. Our high percentage of reversal in Wassermann-fast syphilis is not taken with any degree of conclusiveness, for permanence cannot be judged as yet.

We sincerely believe that bismarsen has shown itself equal to the demands that we first outlined for its future. Its proper utilization should break down those barriers that have heretofore stood in the path of efficient and adequate treatment for the syphilitic infant and child.

THE SPINAL FLUID IN SYPHILIS

THE CLINICAL SIGNIFICANCE OF THE TOTAL PROTEIN AND GLOBULIN

A PRELIMINARY REPORT

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Increase in the protein content of the cerebrospinal fluid is probably the earliest and the most constant of the abnormalities noted in the fluid under pathologic conditions. The presence of increased amounts of protein constitutes direct evidence of a definite reaction of fundamental importance, rendering diagnosis more accurate.

Hewitt [1] Kafka and Samson,[2] Reznikoff,[3] Neel,[4] Lange [5] and others stated that an increase of protein above the normal is invariably accom-

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Submitted for publication, May 12, 1931.

From the Departments of Dermatology and Syphilology, Lenox Hill Hospital and New York University, and Bellevue Medical College, service of Dr. Howard Fox.

1. Hewitt, Leslie F.: Proteins of the Cerebrospinal Fluid, Brit. J. Exper. Path. **8**:84, 1927.

2. Kafka, V.: Die Eiweissrelation des Liquor cerebrospinalis, Ztschr. f. d. ges. Neurol. u. Psychiat. **106**:54, 1926 Kafka, V., and Samson, K.: Die Eiweissrelation des Liquor cerebrospinalis: Modifikation der Methode, ibid. **115**:85, 1928. Kafka, V.: Die Bedeutung der Bestimmung der Eiweissrelation des Liquor cerebrospinalis für die Pathologie der Syphilis, Dermat. Wchnschr. **88**:332, 1929. Kafka, V., and Samson, K.: Die Bedeutung der Eiweissrelation in der Liquordiagnostik, Deutsche med. Wchnschr. **55**:27, 1929; Die Eiweissrelation des Liquor cerebrospinalis: Die Beziehungen der Ergebnisse der Eiweissrelation zu den übrigen Liquorbefunden, Ztschr. f. d. ges. Neurol. u. Psychiat. **119**:153, 1929. Kafka, V.: Die Zerebrospinalflüssigkeit, Leipzig, Franz Deuticke, 1930, pp. 42 and 46. Samson, K.: Kritische Betrachtungen über Eiweissbestimmungsmethoden im Liquor cerebrospinalis mit besonderer Berücksichtigung der Eiweissrelation, Deutsche Ztschr. f. Nervenh. **108**:276, 1929; Physikalisch-chemische Grundlagen der Mastixreaktion: Gegenseitige Beeinflüssung von Serumweisskörpern und Mastixsuspensionen im alkalischen Bereich, Ztschr. f. d. ges. exper. Med. **60**:1, 1928; Ueber die Natur des Liquorglobulins, Klin. Wchnschr. **7**:963 (May 13) 1928.

3. Reznikoff, Paul: The Action of Proteins and Blood Serum on Colloidal Gold Solutions and Its Quantitative Interpretation, J. Lab. & Clin. Med. **8**:92, 1923.

4. Neel, A. V., and Dickmeiss, P.: Der Diagnostische Wert der Goldsol-Reaktion sowie ein Vergleich zwischen den Kurven bei der Goldsol-Reaktion und Globulin-Totaleiweissbestimmungen in der Cerebrospinalflüssigkeit nach Brandberg-Stolnikow-Ross-Jones-Bisgaard, Ztschr. f. d. ges. Neurol. u. Psychiat. **122**:144, 1929; Diagnostic Value of Colloid Reactions in Cerebrospinal Fluid, Hospitalstid. **73**:697, 1930; abstr., J. A. M. A. **95**:1464 (Nov. 8) 1930. Neel, A. V.: Ueber den Zellen und Eiweissgehalt der normalen Spinalflüssigkeit sowie über die Bedeutung die schwachen pathologischen Veränderungen nachweisen zu können, München.

panied by an increase of the globulins, and that this increase ordinarily is accompanied by positive Wassermann and colloidal reactions. The globulin fraction and its relation to the Wassermann and colloidal reactions will be discussed more fully in this report.

Kafka and Samson [2] maintained that in every case in which there is a positive Wassermann reaction of the spinal fluid, there is also an alteration in the protein content of the fluid. In fact, Neel and Dickmeiss [4] have come to the conclusion after an exhaustive study that the colloidal reactions offer no more information in differential diagnosis than that obtained by the total protein and quantitative globulin determinations. Wullenweber [6] maintained that the colloidal reactions are often difficult to interpret, and that in such cases the total protein gives valuable aid in arriving at a diagnosis.

Lange [7] expressed the opinion that a total protein content of 18 mg. per hundred cubic centimeters or more, is invariably responsible for alterations in the colloidal gold curve. This observer considered of value only those gold solutions that are unchanged by spinal fluid with a normal protein content of from 18 to 19 mg. per hundred cubic centimeters, the reaction being expressly and empirically arranged with this object in view, so that every increase of protein, even as little as to 21 or to 22 mg. per one hundred cubic centimeters must give a plainly discernible positive reaction.

The quantitative determination of the total protein gives the clinician a truer insight as to the degree of pathologic change in neurosyphilis; it also offers a means of confirming and substantiating the laboratory as to the accuracy of the concomitant reactions. When the Wassermann reaction is frequently repeated, especially in patients undergoing treatment, it shows considerable disparity, much more so than the total protein and globulin fractions, which give more consistent values. Furthermore, the protein and globulin tests as measured by scopometry [8] are

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med. Wchnschr. **75**:728, 1928; Ueber psychotische Formen von Encephalitis larvata et atypica, sowie über die Notwendigkeit von Lumbalpunktionen bei Psychosen, zugleich ein Vergleich zwischen den Eiweissbestimmungen in der Spinalflüssigkeit nach Brandberg-Stolnikow-Bisgaard und Sicard Cantaloube und Kafka-Samson, Ztschr. f. d. ges. Neurol. u. Psychiat. **122**:278, 1929.

5. Lange, Carl: Lumbalpunktion und Liquordiagnostik, in Kraus, F., and Brugsch, T.: Spezielle Pathologie und Therapie innerer Krankheiten, Berlin, Urban & Schwarzenberg, 1923, vol. 2, pt. 3, p. 492.

6. Wullenweber, G.: Das Verhältnis der Kolloidreaktion zum Gesamteiweissgehalt im Liquor cerebrospinalis, Deutsche Ztschr. f. Nervenh. **107**:172, 1928.

7. Lange (footnote 5, p. 504).

8. Exton, William G.: Scopometry: A System for Optical Measurement and Study of Colloids and Other Dispersions, Arch. Path. **5**:49 (Jan.) 1928; The Junior Scopometer, J. A. M. A. **92**:708 (March 2) 1929; The Photo-Electric Scopometer, Proc. A. Life Insur. M. Dir. America **16**:141, 1929. Exton, W. G., and Rose, A. R.: Clinical Determination of the Albumin Globulin Ratio in Spinal Fluid, J. A. M. A. **96**:36 (Jan. 3) 1931.

exceedingly simple and are therefore less subject to technical error than either the Wassermann or a colloidal reaction. Lastly, these tests serve as a check on therapy and are of prognostic significance, since the protein usually diminishes when treatment and drainage are regularly carried out. Examination of the accompanying case reports will readily show these facts.

Lange [5] emphasized the point that in no case must a quantitative protein estimation of the spinal fluid be omitted; he considers such a determination obligatory and of first importance. Kafka,[2] Ayer and Foster,[9] Wolffheim [10] and numerous others offered similar opinions.

Most investigators up to the present time have been hampered by the sparseness of spinal fluid obtained by lumbar puncture. By suboccipital puncture,[11] however, sufficient spinal fluid is available to permit one to determine the total protein and globulin fractions, in addition to making the usual tests necessary in syphilis; subsequent reexamination of the spinal fluid for verification is also readily made possible by this procedure. The correlation of the results of one spinal fluid examination with the clinical findings often leads to false deductions, and it is only after repeated examination of the spinal fluid that clinical findings and serologic tests can be properly interpreted and evaluated.

It is not my intention to describe or evaluate the various methods for determining the total protein in the spinal fluid, as this work has already been done and published by many observers. In table 1 are enumerated most of the various procedures in use up to the present time for determining the total protein, the year in which these tests first appeared and the high, low and average protein values given by each observer.

Although the gravimetric and Kjeldahl methods are the most accurate in determining the total protein content of the spinal fluid, all

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TABLE 1.—*The Total Protein Values of the Spinal Fluid as Determined by Various Observers*

Observer	Reagent	Method	Mg. of Protein per 100 Cc.			Comment
			High	Low	Average	
Nissl: Centralbl. f. Nervenh. u. Psychiat. **27**: 225, 1904	Esbach's	Volumetric	..	..	..	Expressed in "Teilstriche"
Mestrezat: Le liquide cephalo-rachidien, Paris, Norbert Maloine, 1912, p. 12	Trichloracetic acid 30%	Diaphanometric	32	6	19	Scale of standards
Brandberg, Stolnikow and Roberts: Handbuch der chemischen Analyse, Berlin, Julius Springer, 1924, p. 749	Nitric acid 28%; ring test	Progressive dilutions with NaCl solution	..	..	..	Expressed in dilution figures
Sicard and Cantalaube: Presse méd. **24**: 388, 1916	Trichloracetic acid 30%	Volumetric	24	20	22.5	Rachialbuminimetre
Eskuchen: Die Lumbalpunktion, Berlin, Urban and Schwarzenberg, 1919, p. 50	Picric acid	Volumetric	25	20	22.5	Improved Nissl
Ayer and Foster,[9] 1921	Sulphosalicylic acid 5%	Denis and Ayer[10] colorimetric	38	16	25	Scale of standards
Lange,[5] 1923	Sulphosalicylic acid, agar solution and barium sulphate	Diaphanometric and colorimetric	19	18	..	Over 25 pathologic conditions
Fremont-Smith and Ayer,[9] 1924	Sulphosalicylic acid 5%	Denis and Ayer[10] colorimetric	40	20	30	40 distinct pathologic conditions
Ling: J. Biol. Chem. **69**: 397, 1926	Standard tyrosine solution	Colorimetric	37.9	18.8	25.5	
Kafka and Samson,[2] 1926	Esbach's	Refined volumetric	28.8	19.2	24	Improved Nissl
Custer: München. med. Wchnschr. **32**: 1324, 1926	Sulphosalicylic acid 20%	Diaphanometric	No values given			Scale of standards
Hewitt,[3] 1927	Modified Wu for plasma proteins	Colorimetric	..	..	20	
Halfer: München. med. Wchnschr. **75**: 1628, 1928	Ninhydrin solution 1%	Colorimetric	24	18	21	
Neel and Dickmeiss,[4] 1929	Nitric acid	Brandberg, Stolnikow and Roberts	Expressed in dilution figures			Slightly lower values than obtained by Sicard and Cantalaube
Halpern: Ztschr. f. d. ges. Neurol. u. Psychiat. **121**: 283, 1929	Modified Howe	Kjeldahl	20	27.5	24.6	
Matz and Novick: J. Lab. & Clin. Med. **15**: 370, 1930	Tyrosine solution; modified Wu	Colorimetric	52	21	34	
Wullenweber,[6] 1930	Custer method		20	10	15	Over 30 pathologic conditions
Berger: Klin. Wchnschr. **9**: 888, 1930	Sulphosalicylic acid	Colorimetric	..	5-8	20	Casein solution; "titrocomparator"
Penfold and Irving: M. J. Australia **1**: 772, 1930	Trichloracetic acid	Refractometric	..	..	24	Zeiss refractometer
Young and Bennett: Arch. Neurol. & Psychiat. **23**: 542 (March) 1930	Tsuchiya's reagent	Volumetric	20	5	12.5	Phosphotungstic acid 1.5%
Wolffheim,[10] 1930	.....	Photometric	25	20	22	Zeiss Pulfrich photometer

methods used up to the present time, whether volumetric, diaphanometric, colorimetric or nephelometric, have required considerable time for evaluation, and they have not been clinically applicable, except the method of Denis and Ayer.[9] The Zeiss Pulfrich photometer used by Wolffheim,[10] a photometric method, is the latest to appear. It is of unquestionable value and also clinically applicable.

Following the publication of Exton's work on scopometry, I took up this method for the clinical determination of the total protein and also the recent quantitative globulin method of Exton and Rose [8]. These methods are simple and rapid enough for clinical application.

THE TOTAL PROTEIN TEST

Equal volumes (2 cc.) of spinal fluid are mixed with a 5 per cent sulphosalicylic acid solution containing 10 per cent sodium sulphate.[12]

The mixture is allowed to stand in a suitable test tube with a diameter of 12 mm. for about three minutes; the resulting turbidity is then read in the scopometer. The accuracy of this method when checked against that of Kjeldahl shows a much better agreement than has been obtainable with the various nephelometric methods.

Zaloziecki [13] and Memmesheimer [14] stated that the spinal fluid from the lumbar region contained more protein than that obtained from the cisterna magna. However, Baumann,[15] Weigeldt,[16] Saunders and Spiegel,[11] Ayer and Solomon [9] and others were not of this opinion; they found that in cases of syphilis the biologic reactions of the spinal fluid are practically identical, whether the fluid is taken from the lumbar or from the suboccipital region.

Greenfield and Carmichael,[17] Halpern,[18] Zaloziecki [13] and Young and his co-workers [19] stated that the protein values differed when

12. This substance is known as Exton's reagent and may be obtained from the Eastman Kodak Company, Rochester, N. Y.

13. Zaloziecki, Alex: Ueber den Eiweissgehalt der Zerebrospinalflüssigkeit, Deutsche Ztschr. f. Nervenh. **47**:783, 1913.

14. Memmesheimer, A. W.: Für Bewertung der Reaktionen im Suboccipital gewonnen Liquor cerebrospinalis, München. med. Wchnschr. **74**:1490, 1927.

15. Baumann, W.: Vergleichende Untersuchungen des bei Zisternenpunktion und Lumbalpunktion entnommenen Liquors, München. med. Wchnschr. **74**:148, 1927.

16. Weigeldt, W.: Studien zur Physiologie und Pathologie des Liquor cerebrospinalis, Jena, Gustav Fischer, 1923, p. 89.

17. Greenfield, J. G., and Carmichael, E. A.: The Cerebro-Spinal Fluid in Clinical Diagnosis, London, The Macmillan Company, 1925, p. 221.

18. Halpern, Fanny: Ueber Stickstoff Eiweissverhältnisse im Liquor cerebrospinalis, Ztschr. f. d. ges. Neurol. u. Psychiat. **121**:283, 1929.

19. Young, G. A.; Bennett, A. E.; Christlieb, J. M., and Myers, J. T.: Quantitative Estimation of Total Protein of Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **23**:542 (March) 1930.

various reagents were used to precipitate the spinal fluid. However, when the upper normal values of the various methods as presented in table 1 are averaged, the average is found to be 22.4 mg. of protein per hundred cubic centimeters. According to Samson,[2] most investigators agree as to the approximate upper limit of normal values, and have placed it at about 20 mg. per hundred cubic centimeters. Lange [7] put the upper normal values at from 18 to 19 mg. per hundred cubic centimeters and considered 25 mg. distinctly pathologic. All methods give only relative values; however, they are of sufficient accuracy for clinical interpretations.

The upper limits of "normal" cannot be established at any definite figure. When one approaches a zone the upper limit of which is 18 mg. per hundred cubic centimeters of total protein, I believe that the fluid becomes potentially abnormal and presents presumptive evidence of beginning pathologic change. Fluid of this kind is invariably accompanied by a definite increase in globulin, and the concomitant reactions are also invariably altered. A positive reaction or rather an increase of protein and globulin above approximate normal values should suggest immediate reexamination of the fluid if the other reactions are reported negative. A perusal of the accompanying case reports will illustrate these facts.

MATERIAL STUDIED AND METHOD OF PROCEDURE

The persons studied were patients from the department of dermatology and syphilology of the Lenox Hill Hospital Dispensary and also patients suffering from either clinical neurosyphilis or asmpytomatic neurosyphilis discovered through routine examination who had been discharged from the hospital and referred to the dispensary for further treatment. Patients who have advanced cases of neurosyphilis with psychotic symptoms are seldom met with in this clinic.

This paper deals with 937 examinations of spinal fluids made in 310 cases. Up to the present time, 840 total protein and 587 globulin determinations have been made; 227 of these examinations are tabulated in detail in the accompanying tables and in the 10 case reports. As already mentioned, all spinal fluid was obtained by suboccipital puncture. A sufficient quantity was taken to my office, where I made the total protein and globulin tests. The remainder of the fluid was sent to the laboratory, where a cell count and Pandy, Wassermann [20] and colloidal [21] gold tests were made.

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20. In the Wassermann reaction, titers of from 0.1 to 1 cc. are used with both alcoholic and cholesterolized guinea-pig heart antigens and icebox fixation.

21. All colloidal gold solutions are tested against a known normal and a known paretic fluid before they are used. A colloidal curve of 01210 has very little significance and is usually disregarded.

To establish "normal" values, I obtained spinal fluid from apparently healthy persons who requested that not only a Wassermann test of the blood but an examination of the spinal fluid be made because some member of the family was suffering from neurosyphilis. Other "normals" consisted of patients who presented no evidence of organic disease of the central nervous system as far as could be ascertained, but who were being treated for various skin diseases unrelated to the central nervous system, and who were in the age periods during which syphilis is most often contracted. These cases are tabulated in table 2. In this series of fifteen cases, eighteen examinations of the spinal fluids were made. The total protein ranged from 7 to 21 mg. per hundred cubic centimeters, the average being 11 mg. There was agreement in all of the tests, except in case 7 in which globulin was found and in which

TABLE 2.—*The Proteins of the Cerebrospinal Fluid in "Normal" Patients*

No.	Diagnosis	Age	Cells	Pandy Reaction	Mg. of Protein, per 100 Cc.	Mg. of Globulin, per 100 Cc.	Wassermann Test Negative with 1 Cc.	Colloidal Gold Curve
1	Preputial herpes	25	0	0	7	0	0	0000000000
2	Request	30	0	±	8	0	0	1110000000
3	Preputial herpes	25	5	0	9	0	0	0000000000
4	Lichen planus	28	0	±	10	0	0	0000000000
5	Preputial herpes	33	5	0	15	0	0	0000000000
6	Preputial herpes	31	0	0	9	0	0	0000000000
7	Varicose eczema	56	1	0	21	1	0	0011000000
8	Preputial herpes	28	0	0	10	0	0	0000000000
9	Dermatophytosis	37	1	0	8	0	0	0000000000
10	Varicose eczema	46	2	0	11	0	0	0000000000
11	Preputial herpes	27	2	0	9	0	0	0000000000
12	Preputial herpes*	19	0	0	15	0	0	0001100000
13	Dermatophytosis*	26	0	0	15	0	0	0000000000
14	Request	39	0	0	9	0	0	0010000000
15	Preputial herpes	21	0	±	14	0	0	1112100000

* Described in the case reports.

the total protein reached 21 mg. The other tests were negative. Although this patient was selected as a "normal" control, he was suffering from nephritis with arteriosclerosis, and he was past the age period during which syphilis is usually contracted.

In table 3 are listed the results of forty-nine examinations of the spinal fluid of hospitalized patients and of patients with a questionable history of syphilis for whom such an examination was requested in order to exclude neurosyphilis. Although it is evident that one examination does not rule out this possibility, these findings with the final or tentative diagnoses are herewith tabulated. The presence of protein in cases 7 and 8 is due to arteriosclerotic changes incident to age and hypertension. The presence of globulin, as shown in cases 10, 20, 30 and 37, is usually observed in these pathologic conditions, and at times offers great difficulties in differential diagnosis.

TABLE 3.—*The Proteins of the Cerebrospinal Fluid in Hospitalized Patients and Patients with a Questionable History of Syphilis for Whom a Spinal Fluid Examination Was Requested in Order to Exclude Neurosyphilis*

No.	Diagnosis	Age	Cells	Pandy Reaction	Mg. of Protein, per 100 Cc.	Mg. of Globulin, per 100 Cc.	Wassermann Test Negative with 1.0 Cc.	Colloidal Gold Curve	Comment
1	Chronic cystitis	29	0	±	6	..	0	0011000000	Neurotic symptoms
2	Vague history of syphilis.	23	0	±	5	0	0	0000000000	Treated by a charlatan
3	Hernia	23	0	0	4	0	0	0001000000	
4	Tonsillectomy	49	0	0	11	0	0	0000000000	Neurotic symptoms following operation
5	Vague history of syphilis.	29	0	0	7	0	0	0000000000	Treated by a charlatan
6	Pleurisy	48	2	0	8	0	0	0011000000	
7	Diabetes mellitus	57	0	0	22	0	0	0011100000	
8	Nephritis	49	0	±	23	0	0	0000000000	Arterial hypertension
9	Multiple sclerosis	52	0	0	9	0	0	0000000000	
10	Spinal cord tumor	45	1	0	18	1+	0	0000000000	Fourth lumbar region
11	Vague history of syphilis.	39	0	0	7	0	0	0000000000	Treated by a charlatan
12	Iritis	60	4	0	8	0	0	0110000000	No history of syphilis
13	Otitis media	48	0	0	8	0	0	0000000000	Vague history of syphilis
14	Hematoma on lower leg	33	0	0	8	0	0	0000000000	Vague history of syphilis
15	Cystic ovary	26	0	0	11	0	0	0000000000	Vague history of syphilis
16	Vague history of syphilis.	34	0	0	5	0	0	0000000000	Neurotic symptoms
17	Senile psychosis	66	0	±	16	0	0	0000000000	
18	Vague history of syphilis.	24	0	0	10	0	0	0000000000	
19	Encephalitis	62	0	0	9	0	0	0000000000	
20	Spinal cord condition	20	15	±	14	2	0	0000000000	Undiagnosed
21	Senile psychosis	55	0	0	14	0	0	0000000000	
22	Myocarditis	51	7	0	15	0	0	0000000000	
23	Ulcer of cornea	47	0	0	8	0	0	1222221000	
24	Vague history of syphilis.	48	2	0	13	0	0	0122100000	
25	Multiple sclerosis	36	0	0	10	0	0	0000000000	
26	Vague history of syphilis.	19	0	0	10	0	0	0000000000	
27	Vague history of syphilis.	37	2	0	13	0	0	0000000000	
28	Vague history of syphilis.	47	0	0	13	0	0	0000000000	
29	Alcoholism	32	1	0	10	0	0	0000000000	
30	Nephritis	30	2	0	13	2	0	0000000000	Hemiplegia
31	Epilepsy	10	0	0	10	0	0	0000000000	
32	Vague history of syphilis.	40	2	0	9	0	0	0000000000	
33	Vague history of syphilis.	35	0	0	10	0	0	0000000000	
34	Hemiplegia	62	0	0	14	0	0	0000000000	
35	Malingerer	69	0	0	12	0	0	0000000000	
36	Vague history of syphilis.	34	0	0	9	0	0	0000000000	
37	Encephalitis	37	1	±	18	1+	0	0000000000	
38	Periostitis of tibia	40	1	0	8	0	0	0000000000	
39	Epilepsy	30	7	0	12	0	0	0111000000	
40	Glaucoma	42	0	0	6	0	0	0000000000	
41	Hemiplegia	68	0	0	11	0	0	0000000000	
42	Glaucoma	33	0	0	11	0	0	0011000000	
43	Nephritis	46	0	0	11	0	0	0000000000	Hypertension
44	Epilepsy	41	1	0	12	0	0	0000000000	
45	Duodenal ulcer	44	1	0	12	0	0	0000000000	
46	Nephritis	54	7	0	12	0	0	0012110000	Hypertension
47	Encephalitis	25	5	0	12	0	0	0011000000	
48	Glioma of cord	56	1	0	12	0	0	0000000000	
49	Chronic myocarditis	49	1	0	11	0	0	0011000000	

THE PROTEINS OF THE CEREBROSPINAL FLUID

Group 1: Treated Cases of Early Syphilis.—Table 4 shows that the Wassermann reaction of the blood was negative and results of the dark-field examination were positive. These patients were under treatment and observation for from six months to three years. The spinal fluid

TABLE 4.—*Group 1: Treated Cases of Early Syphilis* *

No.	Number Examinations	Cells	Pandy Reaction	Mg. of Protein, per 100 Cc.	Mg. of Globulin, per 100 Cc.	Spinal Fluid Wassermann per 100 Cc.	Colloidal Gold Curve
1	1	2	0	16	0	0	0000000000
2	1	1	0	10	0	0	0000000000
3	2	2	0	10	0	0	0000000000
4	1	7	±	9	0	0	0000000000
5	2	0	0	8	0	0	0000000000
6	1	1	0	10	0	0	0011000000
7	1	0	0	8	0	0	0000000000
8	3	5	0	8	0	0	0011000000
9	3	0	0	11	0	0	0000000000

* In this group, the Wassermann test of the blood was negative, and results of the dark-field examination were positive.

TABLE 5.—*Group 2: Treated Cases of Early Syphilis*

No.	Number of Examinations	Cells	Pandy Reaction	Mg. of Protein, per 100 Cc.	Mg. of Globulin, per 100 Cc.	Spinal Fluid Wassermann with 1.0 Cc.	Colloidal Gold Curve
1	1	1	0	13	0	0	0000000000
2	2	0	0	8	0	0	0010000000
3	1	0	0	8	0	0	0111000000
4	1	0	0	12	0	0	0000000000
5	1	0	0	12	0	0	0000000000
6	1	2	0	13	0	0	0000000000
7	1	0	0	7	0	0	1221100000
8	2	2	0	9	0	0	0011000000
9	1	5	0	8	0	0	0000000000
10	1	0	0	10	0	0	0000000000
11	2	0	0	5	0	0	0011000000
12	2	10	0	0	0	0	0000000000
13	2	0	0	12	0	0	0010000000
14	1	5	0	5	0	0	0000000000
15	1	7	±	13	0	0	0022322100
16	3	0	0	10	0	0	0134221000
17	1	1	0	10	0	0	0011100000
18	3	0	0	8	0	0	0000000000
19	3	0	0	11	0	0	0000000000
20	1	0	0	6	0	0	0000000000
21	1	2	±	10	0	0	0000000000
22	2	0	0	10	0	0	1111000000

was examined no earlier than six months from the date of infection. In this series of nine cases, 15 examinations of the spinal fluids were made. The total protein ranged from 8 to 16 mg. per hundred cubic centimeters, the average being 10 mg. These nine cases may be considered as representing normal values.

Group 2: Treated Cases of Early Syphilis.—Table 5 gives the results for patients who came under treatment in the early stages of the infection and who had been under treatment and observation for

from six months to three years. The spinal fluid was first examined after the Wassermann reaction of the blood became negative. This series comprises twenty-two patients for whom 34 examinations of the spinal fluids had been made. There was agreement in the allied reactions in all but two of the cases, 15 and 16. This disparity was in the colloidal gold solution; the precipitation took place in the middle zone. The total protein ranged from 5 to 13 mg. per hundred cubic centimeters, the average being 10 mg.

Latent Asymptomatic Syphilis.—The group with latent asymptomatic syphilis comprised thirty-seven patients for whom 75 examinations of the spinal fluid had been made. The infection in these cases dated back from three to thirty years. The Wassermann reaction of the blood was found to be positive, but otherwise the patients were asymptomatic. The total protein ranged from 7 to 23 mg. per hundred cubic centimeters, the average being 12 mg. There was agreement in all of the other reactions, except in ten cases in which the globulin fraction varied from 1 to 5 mg. per hundred cubic centimeters; in six of these cases the total protein varied from 17 to 23 mg. per hundred cubic centimeters. In four cases, the total protein value was 15 mg. per hundred cubic centimeters. In these ten cases the concomitant reactions were negative. The slight increases in the total protein and the presence of globulin as shown by the Exton-Rose scopometric test [8] seem to be the earliest signs of abnormal fluids in cases of Wassermann-fast latent asymptomatic syphilis.

"Cured" Syphilis.—In the group with "cured" syphilis the infection dated back from five to thirty years. In this group of eighty-six patients, 165 examinations of the spinal fluid had been made. The total protein varied from 4 to 22 mg. per hundred cubic centimeters, the average being 8.4 mg. There was agreement in all of the concomitant reactions, except in five cases, in which there was a distinct globulin increase of 2 mg. or more and the total protein was also increased beyond the usual normal figures; in these cases, the ages of the patients varied from 55 to 63 years. The presence of the higher protein and globulin values is probably due to arteriosclerotic changes, and similar observations have been noted by Kafka,[2] Wullenweber [6] and others.

Asymptomatic Neurosyphilis.—In table 6 are shown the results of eighty-seven examinations of the spinal fluids made in fifteen cases for purposes of diagnosis and treatment. The original examination of the spinal fluid which permitted the diagnosis of asymptomatic neurosyphilis was made as part of a routine examination of the blood and spinal fluid during the patient's stay in the hospital for some condition unrelated to the nervous system. Other cases were discovered when patients requested a blood test for an old infection. In most of these

cases the date of infection is unknown; in others, it dates back twenty-five years.

In all of these cases, the total protein was either increased or approached the upper zone of normality, namely 18 mg., or the spinal fluid contained a definite amount of globulin. The increased total

TABLE 6.—*The Proteins of the Cerebrospinal Fluid in Asymptomatic Neurosyphilis*

No.	Blood Wassermann	No. of Examinations	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Spinal Fluid Wassermann 1.0	0.8	0.5	0.2	0.1	Colloidal Gold Curve
1	4+	13	0	1+	21	6	+	..	..	..	..	1243321000
2	4+	15	1	1+	23	6	..	+	..	..	..	2234311000
3	0	15	62	2+	17	4	..	..	..	..	+	0112210000
4	0	2	5	0	12	1+	+	..	..	..	..	2233110000
5	4+	1	30	±	27	6	+	..	..	..	..	1254310000
6	4+	3	17	1+	19	2	±	..	..	..	..	1233100000
7	0	1	3	±	19	2	+	..	..	..	..	1123310000
8	4+	8	1	1+	23	5	..	..	+	..	..	5555433000
9	4+	7	20	±	18	1+	..	..	+	..	..	2334433210
10	4+	8	47	2+	20	2	0	..	..	..	..	0012210000
11	4+	2	0	0	19	2	+	..	..	..	..	0121000000
12	4+	4	55	±	18	2	..	..	+	..	..	0011100000
13	±	3	105	2, 3+	24	3	..	..	..	+	..	2244210000
14	4+	2	30	1+	19	2	..	..	..	+	..	2233310000
15	4+	3	15	±	18	2	..	..	+	..	..	1122100000

TABLE 7.—*The Proteins of the Cerebrospinal Fluid in Meningovascular Neurosyphilis*

No.	Blood Wassermann	No. of Examinations	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Spinal Fluid Wassermann 1.0	0.8	0.5	0.2	0.1	Colloidal Gold Curve
1	4+	21	25	2+	18	5	..	..	+	..	..	1123321000
2	4+	19	5	±	21	6	..	+	..	..	..	1122210000
3	4+	8	6	±	25	9	..	+	..	..	..	0122221000
4	4+	22	1	±	20	5	..	..	+	..	..	2334321000
5	4+	28	8	1+	22	5	..	..	+	..	..	3355433000
6	4+	12	2	0	13	2	0	..	..	..	..	1111000000
7*	4+	7	0	1+	68	18	..	..	..	..	+	5555555321
8*	0	6	5	2+	23	5	+	..	..	..	..	2334210000
9	4+	13	180	2+	35	5	..	+	..	..	..	1221100000
10	4+	5	2	3+	16	2	..	..	+	..	..	1123310000
11	4+	14	0	0	18	5	0	..	..	..	..	2443110000
12	0	13	1	0	15	0	..	+	..	..	..	1221100000
13	0	1	15	1, 2+	11	3	0	..	..	..	..	3322100000
14	3+	1	15	1, 2+	35	4	..	..	+	..	..	2334431000
15	4+	3	45	3+	39	8	..	..	..	+	..	2245522110
16	4+	3	1	±	18	0	..	+	..	..	..	0011000000

* Described in the case reports.

protein and globulin values agree with the other reactions in all of these cases, with the exception of case 10. However, the high cell count verified the protein and globulin findings, and on subsequent examinations of this fluid all of the reactions were in agreement.

Meningovascular Neurosyphilis.—In table 7 are listed the results obtained in a group of 16 patients with meningovascular neurosyphilis for whom 176 examinations of the spinal fluid had been made for diag-

nosis and treatment. The total protein ranged from 13 to 68 mg. per hundred cubic centimeters, the average being 25 mg. The various reactions were in agreement in all but four of the cases: 6, 11, 13 and 16. In these four cases the Wassermann reaction did not agree with the total protein and globulin fractions. This is noted rather often, especially in patients undergoing treatment. The results of subsequent examinations of the spinal fluid were in agreement. In case 13 the patient disappeared from observation after one spinal fluid examination was made.

Early Tabes Dorsalis, Treated and Untreated.—Table 8 shows results in the group of 20 patients with early tabes dorsalis for whom

TABLE 8.—*The Proteins of the Cerebrospinal Fluid in Early Tabes Dorsalis; Treated and Untreated*

No.	Blood Wassermann	No. of Examinations	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Spinal Fluid Wassermann 1.0	0.8	0.5	0.2	0.1	Colloidal Gold Curve
1	4+	12	5	1+	16	6	..	..	+	..	..	1122310000
2*	4+	3	5	±	22	4	..	..	+	..	..	2453210000
3	4+	15	5	±	12	2	..	..	+	..	..	0122100000
4	4+	6	0	0	19	2	+	..	..	..	..	0122100000
5*	4+	4	22	±	20	3	..	..	+	..	..	1122100000
6	4+	15	12	1, 2+	16	5	..	..	..	+	..	4555531000
7	4+	8	0	0	14	2	+	..	..	..	..	1111000000
8	4+	2	4	±	18	5	..	+	..	..	..	1332210000
9	4+	10	0	±	18	3	..	+	..	..	..	0011000000
10	2+	9	12	1+	34	9	..	..	+	..	..	3555421000
11	0	4	7	1, 2+	29	6	..	..	+	..	..	2352210000
12	0	4	5	0	14	0	0	..	..	..	..	0000000000
13	0	2	0	0	8	0	0	..	..	..	..	1221000000
14	4+	4	20	±	23	2	..	..	+	..	..	1122100000
15	0	3	5	1+	19	1+	±	..	..	..	..	3455441000
16	1, 2+	1	1	±	20	1+	0	..	..	..	..	0022110000
17	2+	4	1	0	10	1+	..	..	..	+	..	1222100000
18	4+	1	70	1, 2+	25	3	0	..	..	..	..	3342210000
19	4+	1	22	1, 2+	13	1+	..	..	+	..	..	0111100000
20	4+	1	72	±	23	3	..	..	+	..	..	1112321000

* Described in the case reports.

109 examinations of the spinal fluid had been made for diagnosis and treatment. The total protein ranged from 8 to 34 mg. per hundred cubic centimeters, the average being 18 mg. Globulin was definitely present in all cases, with the exception of cases 12 and 13, in both of which the patients had been under treatment for considerable periods and may be considered as being "cured." In cases 16 and 18, the total protein and globulin fractions did not agree with the Wassermann reaction.

Advanced Cases of Tabes Dorsalis.—Table 9 shows the values for the series of 11 patients with advanced tabes dorsalis in whose cases 18 examinations of the spinal fluid had been made. The total protein ranged from 5 to 19 mg. per hundred cubic centimeters, the average

being 11 mg. The concomitant reactions agreed in all but four of the cases, 2, 3, 4 and 9, in three of which a definite increase in globulin was noted. In case 9, the total protein was slightly increased. These observations agree closely with those of numerous observers.

TABLE 9.—*The Proteins of the Cerebrospinal Fluid in Advanced Cases of Tabes Dorsalis*

No.	Blood Wassermann	No. of Examinations	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Spinal Fluid Wassermann 1.0	0.8	0.5	0.2	0.1	Colloidal Gold Curve
1	0	2	2	±	14	...	±	..	..	..	..	0001100000
2	0	1	0	0	9	3	0	..	..	..	..	0000000000
3	0	1	0	0	10	4	0	..	..	..	..	0011000000
4	0	2	5	±	10	1+	0	..	..	..	..	0000000000
5	0	2	5	0	10	0	0	..	..	..	..	1121100000
6	4+	1	5	0	6	0	0	..	..	..	..	0011100000
7	0	2	0	0	9	0	0	..	..	..	..	0000000000
8	0	1	0	0	11	0	0	..	..	..	..	0000000000
9	0	3	2	±	19	0	0	..	..	..	..	0001000000
10	0	1	0	0	5	0	0	..	..	..	..	0010000000
11	4+	2	1	0	8	0	0	..	..	..	..	0000000000

TABLE 10.—*The Proteins of the Cerebrospinal Fluid in Tabes Dorsalis with Optic Atrophy: Early and Late—Treated and Untreated*

No.	Blood Wassermann	No. of Examinations	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Spinal Fluid Wassermann 1.0	0.8	0.5	0.2	0.1	Colloidal Gold Curve
1	4+	16	5	0	14	2	..	..	+	..	..	0000000000
2†	4+	5	5	1+	21	6	..	..	+	..	..	4455322100
3*†	4+	5	77	2, 3+	35	4	..	..	..	+	..	1222100000
4	4+	10	0	0	14	0	0	..	..	..	..	0000000000
5†	4+	1	0	±	30	...	0	..	..	..	..	.....
6†	4+	2	45	1, 2+	25	7	..	..	..	+	..	1233110000
7	4+	8	5	0	12	1+	0	..	..	..	..	1122000000
8†	4+	4	27	2, 3+	20	5	..	..	+	..	..	1332110000
9†	4+	4	45	2+	31	5	..	..	..	..	+	0122210000
10†	0	1	0	0	20	1+	0	..	..	..	..	0011000000
11	4+	1	20	±	10	0	0	..	..	..	..	0111000000
12	0	1	2	±	9	0	0	..	..	..	..	0112200000
13	4+	6	7	±	16	1+	+	..	..	..	..	0012100000
14	0	1	0	0	10	0	0	..	..	..	..	0000000000
15†	0	1	2	±	18	2	0	..	..	..	..	0021100000

* Described in the case reports.
† Early cases.

Tabes Dorsalis with Optic Atrophy, Early and Late, Treated and Untreated.—Table 10 shows the findings in the series of 15 cases of tabes dorsalis with optic atrophy in which 66 examinations of the spinal fluids had been made for diagnosis and treatment. The total protein ranged from 9 to 35 mg. per hundred cubic centimeters, the average being 19 mg. The Wassermann reaction of the spinal fluid was negative in eight of these cases, and in four of them, cases 7, 10, 13 and 15, there was no correlation with the total protein and globulin fractions.

In cases 1 and 10, the colloidal gold solution did not agree with either the Wassermann reaction or the total protein and globulin fractions. In case 5, some of the spinal fluid was lost.

Ocular Muscle Palsies.—As shown in table 11, the group of cases of ocular muscle palsies consists of 5 patients for whom 51 examinations of the spinal fluid had been made for diagnosis and treatment. The patients in cases 1 and 2 had been under treatment for the past two years, and case 2 represents an end-result. The total protein ranged from 10 to 33 mg. per hundred cubic centimeters, the average being

TABLE 11.—*The Proteins of the Cerebrospinal Fluid in Ocular Muscle Palsies*

No.	Blood Wassermann	No. of Examinations	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Spinal Fluid Wassermann 1.0	0.8	0.5	0.2	0.1	Colloidal Gold Curve
1	4+	14	12	3+	33	16	..	..	+	..	..	2343210000
2	4+	29	0	±	10	0	0	..	..	..	..	0011100000
3	0	2	7	0	19	2	0	..	..	..	..	0000000000
4	0	2	2	0	14	0	0	..	..	..	..	0122100000
5	4+	4	35	±	18	2	..	..	..	+	..	1122100000

TABLE 12.—*The Proteins of the Cerebrospinal Fluid in Dementia Paralytica With Tabes*

No.	Blood Wassermann	No. of Examinations	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Spinal Fluid Wassermann 1.0	0.8	0.5	0.2	0.1	Colloidal Gold Curve
1*	4+	9	17	1, 2+	31	4	0	..	..	..	..	1223311000
2	4+	28	12	2+	27	14	..	..	+	..	..	4555431100
3	4+	1	4	2+	29	6	..	..	+	..	..	4555310000
4*	2+	7	5	±	18	4	..	+	..	..	..	1233100000
5	4+	3	37	4+	41	5	±	..	..	..	..	1555541000
6*	4+	6	85	1+	23	6	..	..	..	+	..	3432100000

* Described in the case reports.

19 mg. The total protein and globulin fractions agreed with the other reactions in all instances except case 3.

Dementia Paralytica with Tabes.—Table 12 shows the findings in the group of 6 cases of taboparesis in which 54 examinations of the spinal fluids had been made for diagnosis and treatment. The total protein ranged from 18 to 41 mg. per hundred cubic centimeters, the average being 34 mg. The globulin ranged from 4 to 14 mg. per hundred cubic centimeters, and in case 2 slightly exceeded the albumin fraction. The total protein and globulin fractions agreed with the other reactions in all the cases except case 1, but on reexamination of the spinal fluid the concomitant reactions were in agreement.

Early General Paralysis.—Table 13 shows observations made in 4 cases of general paralysis in which 20 examinations of the spinal fluids were made. The total protein ranged from 21 to 36 mg. per hundred cubic centimeters. The globulin ranged from 9 to 15 mg. per hundred cubic centimeters, and in case 2 exceeded the albumin fraction. The protein and globulin fractions were in agreement with all of the other tests.

THE GLOBULIN OF THE SPINAL FLUID IN SYPHILIS

The Globulin Tests.—The various so-called globulin tests (Pandy,[22] Ross-Jones,[23] Noguchi,[24] Weichbrodt[25] and Nonne-Apelt-Schumm[26]) for the quantitative determination of protein are generally conceded to be unsatisfactory. The reading of the results of these tests involves the personal equation to so great an extent that the tests become unreliable for comparative purposes. Stokes[27] was of the opinion

TABLE 13.—*The Proteins of the Cerebrospinal Fluid in Early Dementia Paralytica*

No.	Blood Wassermann	No. of Examinations	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Spinal Fluid Wassermann 1.0	0.8	0.5	0.2	0.1	Colloidal Gold Curve
1	4+	11	2	2+	36	11	..	..	..	+	..	5555531000
2	4+	4	2	1+	21	15	..	+	..	..	..	2554431000
3	4+	4	5	3+	27	12	..	..	..	+	..	5555310000
4	4+	1	6	±	31	9	..	..	+	..	..	5555543210

that they are of limited diagnostic value and of no great prognostic significance.

Furthermore, as Pandy,[22] Kafka and Samson,[2] Nonne,[26] Denis and Ayer,[9] Exton[8] and others have shown, these tests are not specific for either globulin or albumin, with the exception of the Nonne-Apelt-Schumm[28] reaction. However, the latter must be interpreted not later than three minutes after the fluids have been mixed, otherwise the albumins are also precipitated. In the case reports submitted from

22. Pandy, K.: Ueber eine neue Eiweissprobe für die Cerebrospinalflüssigkeit, Neurol. Centralbl. **29**:915, 1910.

23. Ross, G. W., and Jones, Ernst: On the Use of Certain New Chemical Tests in the Diagnosis of General Paralysis and Tabes, Brit. M. J. **1**:1111, 1909.

24. Noguchi, Hideyo: The Relation of Protein, Lipoids and Salts to the Wassermann Reaction, J. Exper. Med. **11**:84, 1909.

25. Weichbrodt, R.: Eine einfache Liquorreaktion, Monatschr. f. Psychiat. u. Neurol. **40**:349, 1916.

26. Nonne, Max: Syphilis und Nervensystem, Berlin, S. Karger, 1924, p. 126.

27. Stokes, John H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1926, pp. 104 and 966.

28. Nonne (footnote 26, p. 127 to 128).

the laboratory, one can readily see the inexactness of the Pandy reaction in interpreting globulin increase, as compared with this newer method of evaluating the globulin fraction by the Exton-Rose scopometric test.

According to Lange,[29] Exton and Rose,[8] phenol shows the presence of globulin in smaller concentrations than it does albumin. If equal concentrations of albumin and globulin are precipitated separately with phenol, the globulin precipitate will be denser than the albumin precipitate. Therefore it is possible to get positive phenol tests with relatively less globulin than albumin, and negative phenol tests with relatively more albumin than globulin. Moderate and large amounts of albumin give strong phenol reactions, even in the complete absence of globulin. Therefore, a phenol test made directly on the spinal fluid does not admit of interpretation as regards either the amount of albumin or the amount of globulin. While there is justification for suspecting the presence of globulin in the majority of instances in which such tests as Pandy's are positive, it is nevertheless unquestionable that no differential protein test is specific unless it is based on protein fractionation. The Weichbrodt [25] and the Noguchi [24] tests are similarly nonspecific for globulin, according to Lange [30] and Kafka and Samson.[2]

The Globulin Fraction.—While the exact chemical composition of nearly all of the proteins is as yet unknown, the separation into the fractions, namely albumins and globulins, by half saturation with ammonium sulphate is universally accepted and regarded as classic. Such a qualitative application to spinal fluid is known as the Nonne-Apelt-Schumm test. The Exton-Rose method makes use of this fractionation and is more than sufficiently accurate for clinical interpretation.

Nonne [26] expressed the opinion that his test is positive in at least 95 per cent of cases of syphilitic disease of the central nervous system. Lange,[31] Zaloziecki,[13] Pappenheim,[32] Wullenweber [6] and Bisgaard [33] maintain that a positive Nonne test denotes a definite pathologic increase of the total protein. Furthermore, according to Lange [31] and also Bisgaard,[33] the Nonne test fails to detect existing pathologic processes when the fluid contains less than 50 mg. per hundred cubic centimeters of total protein. As regards the detection of minimum amounts of globulin, the Exton-Rose method is much more sensitive than any

29. Lange (footnote 5, p. 499).

30. Lange (footnote 5, p. 498).

31. Lange (footnote 5, p. 505).

32. Pappenheim, Martin: Lumbar Puncture, translated by G. Caffrey, London, John Bale Sons & Danielsson, 1925, p. 108.

33. Bisgaard, A.: Methode zu objektiver Schatzung der sogenannten Phase I bei Untersuchungen der Liquor cerebrospinalis, Monatschr. f. Psychiat. u. Neurol. **28**:124, 1910; Die Eiweissuntersuchung der Cerebrospinalflüssigkeit durch 234 Fälle beleuchtet, Ztschr. f. d. ges. Neurol. u. Psychiat. **14**:329, 1913.

of the hitherto existing technics, because the isolated globulin is precipitated under conditions that give it far greater obscuring power, that is, turbidity.

The amount of globulin normally present in the spinal fluid is still under discussion. This determination depends not only on the methods used but on the technical skill of the observer. Many other factors, such as the salt content, the hydrogen ion concentration, the physical state of the protein and other conditions over which one has no control, enter into such a determination. These, however, do not affect the result of the Exton-Rose method when it is properly performed.

In the spinal fluid of only one of fourteen normal persons whose other reactions were negative did Jacobsthal and Joel [34] find globulin. Solomon [35] was of the opinion that normal spinal fluid contains no globulin, but he offers no experimental evidence. Lange [30] and Neel [4] expressed similar views. Neel [4] came to this conclusion after working with the Brandberg-Roberts-Stolnikow-Ross-Jones-Bisgaard test.[36] This method utilizes the principle of Heller's nitric acid ring test for albumin in urine. Similarly, a series of dilutions of spinal fluid and sodium chloride are tested either with 28 per cent nitric acid or with a saturated solution of ammonium sulphate, depending on whether total protein or globulin is being sought. The tested dilutions are compared with a known standard, and the figures are expressed either on a percentage basis or by a dilution figure. The Psychiatric Field Service [37] of the State Board of Control of Wisconsin similarly holds that globulin is either absent or present in a faint trace in normal spinal fluid. Nicholson [38] and Eskuchen [39] stated that normal spinal fluid contains a trace of globulin that is not demonstrable by the ordinary tests.

Hewitt,[1] working with a modified Wu's [40] blood protein method, found that the determination of the euglobulin and pseudoglobulin fraction is difficult. In normal persons the total globulin is about 0.003 per cent, a quantity that is just detectable by this method, and

34. Jacobsthal, Erwin; and Joel, Moritz: Liquor Untersuchungen, Klin. Wchnschr. **40**:1896, 1927.

35. Solomon, H. C.: Nonconcomitance of Spinal Fluid Tests, Arch. Neurol. & Psychiat. **3**:49 (Jan.) 1920.

36. Brandberg, Roberts and Stolnikow: Handbuch der chemischen Analyse, Berlin, Julius Springer, 1924, p. 749.

37. Psychiatric Field Service of the State Board of Control of Wisconsin: Ven. Dis. Inform. **10**:123 (March) 1929.

38. Nicholson, Daniel: Laboratory Medicine, Important Normal Standards, Philadelphia, Lea & Febiger, 1930.

39. Eskuchen, K.: Die Lumbalpunktion, Berlin, Urban & Schwarzenberg, 1919, p. 50.

40. Wu, Hsien: A New Colorimetric Method for the Determination of Plasma Proteins, J. Biol. Chem. **51**:33, 1922.

the euglobulin about 0.0005 per cent, a quantity that cannot be analyzed, especially since the figure is arrived at by difference. Kafka [2] held that euglobulin is absent in normal spinal fluid, but is increased in syphilitic disease of the central nervous system. Halpern,[18] modifying Howe's [41] method for testing blood serum, applied it to spinal fluid and found an average of 10.44 mg. of globulin per hundred cubic centimeters in normal persons. Kafka and Samson,[2] using a complicated and time-consuming method, precipitate the spinal fluid with a saturated solution of ammonium sulphate, centrifugate this globulin precipitate for twenty minutes in special tubes, redissolve this precipitate in saline solution, again precipitate it with Esbach's reagent and again centrifugate it for thirty minutes; they find the globulin values to vary between 2.4 and 4.8 mg. per hundred cubic centimeters in normal persons.

Matz and Novick,[42] using the method of Wu [40] for the estimation of the blood proteins and that of Hewitt [1] for spinal fluid proteins and using a colorimetric technic, found on an average 13 mg. of globulin per hundred cubic centimeters in ten nonmeningitic and nonsyphilitic patients. In all of the normal spinal fluids submitted to them for examination, Exton and Rose [8] found no globulin. Their findings were in agreement with my own. The allied reactions in all of these cases were also negative (table 2).

The Exton-Rose Globulin Test.—The following reagents and glassware should be conveniently at hand: a saturated solution of ammonium sulphate, a saturated aqueous solution of phenol, distilled water, some clean test tubes having a diameter of 12 mm., a dense or hardened filter paper [43] having a diameter of 55 mm. and a small funnel about 60 mm. long, with a diameter of about 30 mm.

1. Equal volumes (2 cc.) of spinal fluid and ammonium sulphate solution are mixed and allowed to stand a few minutes for the globulin to salt out.

2. The mixture is filtered and the filtrate passed through the same filter until it is clear, care being taken to drain the test tube thoroughly. The filtrate is now an albumin solution and may be set aside in case it is desired to precipitate and measure the albumin separately. The salted-out globulin is on the filter paper in the funnel, which is now placed in a clean test tube.

3. Two cubic centimeters of distilled water is poured on the filter paper to bring the globulin into solution, and this is passed three times through the same filter paper so as to insure a homogeneous solution of globulin.

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41. Howe, Paul E.: The Use of Sodium Sulphate as the Globulin Precipitant in the Determination of Proteins in Blood, J. Biol. Chem. **49**:93, 1921; The Determination of Proteins in Blood: A Micro Method, ibid., p. 109.

42. Matz, P. B., and Novick, Nathan: Improved Colorimetric Procedure for the Quantitative Estimation of the Protein of the Cerebrospinal Fluid, J. Lab. & Clin. Med. **15**:370 (Jan.) 1930.

43. A hardened paper is much slower than a dense paper, but the filtrate need not be passed through the funnels so many times. I use either Whatman no. 50 or Carl Schleicher and Schull no. 575.

4. After the funnel has been thoroughly drained, 0.2 cc. of distilled water is added in the tip of the filter cone to wash down the globulin that adheres to the tip of the cone.

5. One cubic centimeter of ammonium sulphate solution is added to the globulin solution and mixed.

6. The globulin is precipitated by adding 3 cc. of the phenol solution and mixed by gently inverting the tube once (it should not be shaken). The globulin phenol precipitate is allowed to stand for at least fifteen minutes without being disturbed and the turbidity is read in the scopometer between fifteen and thirty minutes after precipitation. The number of milligrams of globulin per hundred cubic centimeters of spinal fluid is then obtained by dividing the junior scopometer scale reading by 4.

7. The albumin is obtained by subtracting the globulin from the total protein. If a separate precipitation of the albumin is desired, 1 cc. of distilled water is mixed with 2 cc. of the original ammonium sulphate filtrate and precipitated with phenol in the manner employed for globulin. The number of milligrams of albumin per hundred cubic centimeters of spinal fluid is then obtained by dividing the junior scopometer scale reading by 2.

Owing to the minute quantities of globulin present in the spinal fluid, different observers have endeavored to detect these small fractions by various methods. Lange [44] reduces the volume of the spinal fluid in vacuum and then precipitates this concentrated solution with a saturated ammonium sulphate solution. Kahn [45] adds a small quantity of talc to the mixture of spinal fluid and saturated ammonium sulphate solution to facilitate bringing down the globulin while centrifugating for fifteen minutes. After the supernatant fluid is poured off as completely as possible, the precipitate is suspended in 0.3 cc. salt solution, and this suspension is centrifugated. The test is completed with the supernatant fluid that contains the dissolved globulin. In their new test, Exton and Rose [8] produced a complete precipitation or dispersion of the globulin fraction so that these finer and sensitive reactions may be evaluated by scopometry, thereby not only insuring greater accuracy but putting the globulin determination on a measurable basis similar to the total protein test. I have indicated minute increases of globulin by the figure 1 plus. This includes dispersions up to 2 mg., as from there on the scale readings on the junior scopometer [8] are more readily appraised and offer no difficulty in reading.

Patients with asymptomatic syphilis who present themselves to ascertain whether they have neurosyphilis and who present minute increases of globulin, a total protein approaching the zone of 18 mg. per hundred cubic centimeters and negative concomitant reactions have not been studied sufficiently long to enable one to arrive at any definite conclusion. In a subsequent study, with the aid of the photo-electric

44. Lange (footnote 5, p. 494).

45. Kahn, R. L.: Serum Diagnosis of Syphilis by Precipitation, Baltimore, Williams & Wilkins Company, 1925, p. 154.

scopometer,[8] I expect to report more fully on this type of case. The detection of these sensitive reactions may be the first diagnostic criterion for neurosyphilis.

The Importance of the Globulin Fraction.—Kahn [45] as has been mentioned, utilizes the globulin fraction of the spinal fluid in determining his precipitation test for syphilis, and other observers, Hull and his co-workers,[46] Keim and Kahn,[47] McDermott,[48] Herrold,[49] and Davenport [50] claim greater sensitivity for this method.

Cruickshank [51] held that the substances in the spinal fluid that cause the precipitation of the colloidal gold are not dialyzable and reside in the globulin fraction of the protein, and in this respect resemble the Wassermann-reacting substances. Hewitt [1] was of the opinion that in pathologic fluids all the proteins are increased in quantity, but chiefly globulin, and that the colloidal gold precipitation is governed by the albumin and globulin content. Neel and Dickmeiss [4] and Kafka and Samson [2] stated that when the globulin is considerably increased, as in dementia paralytica, the greatest precipitation of the gold solution will take place in the first or paretic zone. If the amount of globulin is not so great, the precipitation will take place in the middle zone, and as the globulin diminishes the precipitation of the gold solution decreases. Samson [2] stated the opinion that it is the globulin fraction of the protein that comes into play with the colloidal reactions, and that it is still questionable whether the globulins are directly responsible for these colloidal reactions or some combination of bodies in the reaction. That it is due to the different globulins in the fluid seems certain, but how it works is unknown. Reznikoff,[3] Jacobsthal and Joel [34] were of a similar opinion.

There seems to be little doubt from the work of Noguchi,[24] Harold,[52] Herrold,[49] Kafka and Samson,[2] Hewitt,[1] and the other investigators mentioned that the reacting substances responsible for the Wassermann

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46. Hull, Thomas G.; Fry, L., and Garwood, C.: The Kahn Test on Spinal Fluid, Am. J. Syph. **12**:104 (Jan.) 1928.

47. Keim, H. L., and Kahn, R. L.: Clinical Studies of the Kahn Reaction for Syphilis: III. The Test with Spinal Fluids, J. A. M. A. **84**:881 (March 21) 1925.

48. McDermott, E. B.: The Kahn Presumptive Procedure with Spinal Fluids, Arch. Neurol. & Psychiat. **23**:531 (March) 1930.

49. Herrold, R. D.: The Precipitation Test for Syphilis of Concentrated Arachnoid Fluid and Serum, J. A. M. A. **81**:203 (July 21) 1923.

50. Davenport, Kenneth M.: The Clinical Value of the Kahn Test with Spinal Fluids, Am. J. Syph. **13**:570 (Oct.) 1929. The Clinical Value of the Presumptive Kahn Test with Spinal Fluids, Am. J. Syph. **13**:575 (Oct.) 1929.

51. Cruickshank, John: The Value and Mechanism of the Colloidal Gold Test, Brit. J. Exper. Path. **1**:71, 1920.

52. Harold, C. H. H.: The Euglobulin Group and Its Relationship to the Wassermann Reaction, J. Roy. Army M. Corps **39**:83, 1922.

reaction of the spinal fluid and the substances responsible for the colloidal reactions are contained in the globulin fraction, or, more specifically, in the euglobulin or 33 per cent ammonium sulphate fraction of the spinal fluid.

The importance therefore of evaluating the globulin fraction by the Exton-Rose method and estimating these sensitive dispersions by scopometry becomes evident.

THE ALBUMIN-GLOBULIN RATIO

Kafka [2] maintains that by his method of fractionating the globulins and in conjunction with the determination of the albumin-globulin ratio, he is able to differentiate and diagnose the various syphilitic processes of the central nervous system. Lange,[44] however, is of the opinion that the protein quotient is of little diagnostic value, especially when the protein values are small and when they are determined by chemical analysis, for these determinations are relative, and therefore have no comparative value. I am in agreement with the last mentioned observer. While the total protein values are fairly constant and more of an absolute determination, the globulin fraction varies considerably, so that no definite conclusions can be drawn. Variations exist in the protein and globulin values, depending on the stage and severity of the process and on whether or not treatment had been given before the patients came under observation, so that no definite conclusions can be drawn from such ratios. In severe involvement of the central nervous system, the globulin fraction is materially increased and in some cases may exceed the albumin fraction; when such a condition persists and the globulin fraction remains high, it is distinct evidence of parenchymatous involvement. Neel and Dickmeiss,[4] Wullenweber,[6] Zaloziecki [15] and Kafka and Samson [2] have offered similar opinions. A temporary increase in globulin over albumin is met with in some vascular types of neurosyphilis; however, in most instances such patients respond to therapy. The exact origin of the proteins of the cerebrospinal fluid, whether they are endogenous or exogenous, is still a matter for future investigation.

REPORT OF CASES

Case 1.—H. S., aged 54, a salesman, born in England, who had been in the United States for eighteen years, had been treated for his present condition thirteen years previously and periodically since then. He had a "stroke" about three weeks before this article was written and had lost his speech for about a week. He first came under observation on Sept. 27, 1930. At that time the Wassermann reaction of the blood was 3 plus. The patient complained of pain in the legs, poor memory and hesitating speech. Examination at that time revealed unequal and Argyll Robertson pupils. The optic disks were slightly atrophic. The deep reflexes were absent; ataxia, tremor of the hands and a speech defect were also noted. The diagnosis was dementia paralytica with tabes.

The patient received intensive treatment with spinal drainage. The results of the examinations of the spinal fluid are given in table 14.

Case 2.—D. N., aged 38, a maid, born in Germany, who had lived in the United States for the past seven years, complained of insomnia and was unable to work because of weakness in the legs, trembling and backache. She said that she had been infected twelve years prior to examination and had received little treatment. She first came under observation on Jan. 23, 1931. The Wassermann reaction of the blood was 4 plus. The optical examination revealed unequal and Argyll Robertson pupils. The visual fields, as well as the color fields, were normal. The knee reflexes were absent. The Romberg test was positive. The diagnosis was tabes dorsalis.

Table 14.—*Observations on the Spinal Fluid in Case 1*

Date	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Wassermann Test	Colloidal Gold Curve
9/29/30	17	1, 2+	31	4	Negative with 1 cc.	1223311000
10/ 6/30	17	1, 2+	32	3	Positive with 0.5 cc.	1123310000
10/24/30	20	±	25	5	Positive with 0.5 cc.	2333210000
11/ 7/30	1	±	24	2	Positive with 0.8 cc.	0111100000
12/13/30	12	1+	18	6	Negative with 1 cc.	1453210000
12/20/30	7	1+	24	3	Negative with 1 cc.	1122100000
1/20/31	5	±	19	2	Positive with 0.2 cc.	3344210000
2/21/31	8	1+	21	5	Negative with 1 cc.	1122110000
2/28/31	40	2+	25	3	Positive with 0.8 cc.	1123310000

Table 15.—*Observations on the Spinal Fluid in Case 2*

Date	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Wassermann Test	Colloidal Gold Curve
2/ 6/31	5	±	22	4	Positive with 0.5 cc.	2453210000
2/20/31	20	1+	19	4	Negative with 1 cc.	2233210000
2/27/31	22	2+	18	3	Positive with 1 cc.	3445320000

The patient received intensive treatment with spinal drainage. The results of the spinal fluid examinations are shown in table 15.

Case 3.—J. H., aged 49, an agent, born in Germany, who had lived in New York for the past twenty years, complained of failing sight for the past four months. He was referred from the ophthalmologic department on Sept. 30, 1930, for treatment. The Wassermann reaction of the blood was 4 plus. The patient said that he did not have venereal infection, and had received no treatment for the condition up to the present time. The optical examination revealed unequal and Argyll Robertson pupils. The visual fields were markedly contracted; the results of the color tests were poor. The optic disks were pale and atrophic. The Romberg test was positive; ataxia was present, and the deep reflexes were absent. The diagnosis was optic atrophy and tabes dorsalis.

Intensive treatment with spinal drainage was given. The results of the examinations of the spinal fluid are shown in table 16.

Case 4.—N. A., aged 48, a worker in a garage, born in Russia, who had lived in the United States for the past seven years, said that he had had a chancre during 1912. He received his first treatment in 1925, when the Wassermann

reaction of the blood was found to be positive; since that time he had received various courses of treatment. He was referred for examination of the spinal fluid on June 10, 1930; he subsequently disappeared from observation until December 5, when the Wassermann reaction of the blood was 2 plus. He complained of general weakness and pains in the legs; he had a slight speech defect. Examination at that time revealed unequal and Argyll Robertson pupils. The Romberg test was positive; the deep reflexes were absent, and there was a diminution of the vibratory and deep pain senses. The diagnosis was dementia paralytica with tabes.

The patient received intensive treatment with spinal drainages. The results of examinations of the spinal fluid are shown in table 17.

TABLE 16.—*Observations on the Spinal Fluid in Case 3*

Date	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Wassermann Test	Colloidal Gold Curve
10/ 4/30	77	2, 3+	35	4	Positive with 0.2 cc.	1222100000
10/17/30	27	2, 3+	30	4	Positive with 0.2 cc.	2344420000
11/28/30	7	1, 2+	30	4	Positive with 0.2 cc.	1111210000
12/ 8/30	10	2, 3+	33	3	Positive with 0.8 cc.	1112211000
2/27/31	7	2+	26	4	Positive with 0.5 cc.	1123310000

TABLE 17.—*Observations on the Spinal Fluid in Case 4*

Date	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Wassermann Test	Colloidal Gold Curve
6/10/30	5	±	18	4	Positive with 0.8 cc.	1233100000
12/ 5/30	5	±	16	2	Negative with 1 cc.	5554331000
12/12/30	2	±	20	4	Negative with 1 cc.	5553210000
12/19/30	5	±	21	5	Positive with 0.5 cc.	4555311000
1/16/31	1	1+	17	2	Positive with 0.5 cc.	2443300000
2/20/31	0	0	19	4	Positive with 0.8 cc.	1333210000

TABLE 18.—*Observations on the Spinal Fluid in Case 5*

Date	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Wassermann Test	Colloidal Gold Curve
1/30/31	22	±	20	3	Positive with 0.5 cc.	1122100000
2/ 2/31	15	1+	19	3	Negative with 1 cc.	0011100000
2/ 6/31	10	1+	20	3	Positive with 0.8 cc.	0123220000
3/ 2/31	1	1+	20	1+	Positive with 1 cc.	1223210000

CASE 5.—J. B., aged 49, a mechanic, born in Germany, who had lived in the United States for the past seven years, said that he had had a chancre eighteen years before he consulted me. He received a few rubbings at that time and no other treatment subsequently.

The patient first came under observation on Jan. 15, 1931. At that time the Wassermann reaction of the blood was 4 plus. He complained of insomnia, felt depressed and had pains in the back. Examination revealed unequal pupils; the ankle reflexes were absent, and the knee jerks were diminished. The Romberg test was positive. The diagnosis was tabes dorsalis. The patient received intensive treatment with spinal drainages. The results of the examinations of the spinal fluid are shown in table 18.

Case 6.—R. W., aged 41, a seaman, born in Switzerland, who had lived in the United States for the past fifteen years, said that he had had a chancre fifteen years before I saw him, and that he had received some injections about two years previously; he said that the Wassermann test was negative after he received this treatment.

The patient first came under observation on Nov. 13, 1930, having been referred from the urological department. The Wassermann reaction of the blood was 4 plus. He complained of difficulty in urination. Examination at that time revealed unequal and Argyll Robertson pupils. Vision in the right eye was 8/200; in the left eye, fingers could be distinguished at 6 feet (182 cm.). The reflexes were sluggish in the upper extremities, and the tendon reflexes in the lower extremities were absent. Vibratory sense was preserved. The Romberg test was positive. The patient appeared unusually sluggish, although no demonstrable mental aberration was present. The neurologic diagnosis gave the impression of early dementia

Table 19.—*Observations on the Spinal Fluid in Case 6*

Date	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Wassermann Test	Colloidal Gold Curve
11/18/30	85	1+	23	6	Positive with 0.2 cc.	3432100000
11/28/30	150	3+	40	4	Positive with 0.1 cc.	3322210000
12/ 8/30	57	3+	28	4	Positive with 0.8 cc.	4555321100
1/19/31	3	1+	21	3	Positive with 0.1 cc.	2333100000
2/20/31	0	±, 1+	19	2	Positive with 1.0 cc.	2333210000

Table 20.—*Observations on the Spinal Fluid in Case 7*

Date	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Wassermann Test	Colloidal Gold Curve
11/14/30	10	1+	68	18	Positive with 0.1 cc.	5555555321
11/21/30	7	4+	60	9	Positive with 0.1 cc.	5555321100
12/ 1/30	1	3+	54	6	Positive with 0.2 cc.	5555421000
12/12/30	10	4+	56	11	± with 1.0 cc.	5555532100
12/26/30	2	3+	46	9	Positive with 0.1 cc.	4555321000
2/ 6/31	5	4+	50	9	Positive with 0.5 cc.	3555543200
3/13/31	5	2+	35	6	Positive with 0.5 cc.	3554421000

paralytica with tabes. The patient received intensive treatment with spinal drainage. The results of the examinations of the spinal fluid are shown in table 19.

Case 7.—M. S., aged 39, a widow, born in Poland, who had been in the United States for the past sixteen years, was admitted to the hospital on Oct. 13, 1930, following a hemiplegic seizure. She had previously complained of headaches and dizziness. At the time of presentation, the Wassermann reaction of the blood was 4 plus. The examination of the spinal fluid on Oct. 14, 1930, gave the following results: 75 cells; globulin test, 4 plus; Wassermann reaction, positive with 0.2 cc. of spinal fluid; colloidal gold curve, 4555555211. Examination revealed unequal pupils that reacted sluggishly to light and in accommodation. There was right-sided hemiparesis, and a slurring of speech was noted. The deep reflexes were hyperactive. The diagnosis was vascular neurosyphilis.

The patient was discharged in an improved condition on November 5, and referred to the dispensary for further treatment. She received intensive treatment with spinal drainages. The results of examinations of the spinal fluid are shown in table 20.

CASE 8.—D. A., aged 43, married, a maid, was admitted to the hospital on Sept. 6, 1930, in a comatose condition. She had previously complained of headaches and dizziness. It was noted that she had right-sided paralysis of the facial muscles and also ptosis of the left eyelid. The pupils were unequal and reacted to light and in accommodation. The fundi were normal, and the patient complained of diplopia. The Wassermann reaction of the blood was negative. The examination of the spinal fluid gave the following results: 15 cells; globulin test, 2 plus; Wassermann reaction, positive with 0.2 cc. of spinal fluid; colloidal gold curve, 1123322100. The diagnosis was vascular neurosyphilis.

The patient was discharged in an improved condition on Sept. 19, 1930, and referred to the dispensary for further treatment. She received intensive treatment with spinal drainages. The results of the examinations of the spinal fluid are shown in table 21.

CASE 9.—K. V., aged 19, a bus boy, born in Germany, came to the clinic suffering from a penile lesion that had been present four days. He first came under

TABLE 21.—*Observations on the Spinal Fluid in Case 8*

Date	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Wassermann Test	Colloidal Gold Curve
10/17/30	5	2+	23	5	Positive with 1.0 cc.	2334210000
10/27/30	17	1, 2+	19	3	Positive with 0.5 cc.	1112210000
11/10/30	1	1+	20	3	Positive with 0.5 cc.	0000000000
12/ 5/30	5	2+	29	5	± with 1 cc.	2223331000
2/ 9/31	1	±	21	4	Negative with 1 cc.	1223331000
3/16/31	5	2+	20	2	Positive with 0.5 cc.	0011210000

TABLE 22.—*Observations on the Spinal Fluid in Case 9*

Date	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Wassermann Test	Colloidal Gold Curve
12/30/30	1	±	16	0	Positive with 1 cc.	0000000000
1/24/31	0	0	15	0	Negative with 1 cc.	0001100000

observation on Aug. 9, 1930, when he presented a number of pinhead-sized superficial erosions on the prepuce. Three dark-field examinations gave negative results. The Wassermann reaction of the blood was reported negative on three different examinations. The diagnosis was preputial herpes.

The patient did not object to having an examination of the spinal fluid made.

This patient was selected as a normal control, but as the Wassermann reaction of the spinal fluid was reported positive, and as this report did not agree either with the clinical findings or with the total protein and globulin fractions, the test had to be repeated. The results of the examinations of the spinal fluid are shown in table 22.

CASE 10.—T. P., aged 26, a carpenter, born in Germany, requested that an examination of the blood be made because he was suffering from a cutaneous condition of the hands. He first came under observation on Dec. 13, 1930. He said that he had not had syphilis or any other venereal infection. On examination he presented a papular and vesicular eruption. The lesions were sharply defined and were limited to the fingers and palms of both hands. The diagnosis was dermatophytosis. The Wassermann reaction of the blood was negative on two examinations. The patient did not object to having an examination of the spinal fluid made.

This patient was selected as a normal control, but as the Wassermann reaction of the spinal fluid was reported positive, and as this report did not correlate either with the clinical findings or with the total protein and globulin fractions, the test had to be repeated. The results of the examinations of the spinal fluid are shown in table 23.

TABLE 23.—*Observations on the Spinal Fluid in Case 10*

Date	Cells	Pandy Reaction	Mg. of Protein per 100 Cc.	Mg. of Globulin per 100 Cc.	Wassermann Test	Colloidal Gold Curve
12/30/30	0	0	14	0	Positive with 0.8 cc.	0000110000
1/17/31	5	0	12	0	Negative with 1 cc.	0000000000
1/24/31	0	0	15	0	Negative with 1 cc.	0000000000

SUMMARY AND CONCLUSIONS

1. The importance of quantitatively estimating the total protein and the globulin fraction in spinal fluid is shown in a study of 310 cases, embracing 840 protein and 587 globulin tests.

2. The diagnostic significance of evaluating the total protein and globulin fractions and the changes due to treatment are shown by a practical clinical method.

3. Every examination of the cerebrospinal fluid in syphilis should include a quantitative protein test, because it is a valuable addition to the diagnostic criteria.

4. The total protein estimation should commend itself as a valuable adjunct to the Wassermann reaction, the results of which it is capable of confirming.

5. The upper normal limit of the total protein content of the spinal fluid is about 18 mg. per hundred cubic centimeters.

6. There is a definite parallelism between an increase of the total protein and that of the globulin fraction in most cases.

7. There is no definite agreement of the colloidal gold curve and the Wassermann reaction with the total protein or globulin, although a large increase of globulin forecasts a precipitation of the gold solution in the first or paretic zone.

8. A distinct increase in globulin with a total protein approaching 18 mg. per hundred cc. is evidence of a pathologic spinal fluid in syphilis.

9. Attention is called to the advantages of accurately fractionating and quantitatively determining protein by the simple clinical method of Exton and Rose.

241 West One Hundredth Street.

THE HENAL VACUUM VAPORIZER

AN INSTRUMENT USEFUL IN THE TREATMENT OF CERTAIN MYCOTIC AND PYOGENIC CUTANEOUS DISEASES

ALBERT STRICKLER, M.D.
PHILADELPHIA

During the conduct of an investigation dealing with the various methods and formulas advocated for mycotic infections of the hands and feet, a new instrument, "The Henal Vacuum Vaporizer," based on reorganized physical and physiologic principles and designed primarily for the treatment for fungus infections, was devised in the research laboratories of The Skin and Cancer Hospital of Philadelphia.

The principles on which this instrument is based are the ability to create a vacuum of controllable intensity, with a maximum equivalent to 20 inches (50.8 cm.) of mercury and delivery of the remedy employed in an almost complete vaporized state.

The advantages of the new apparatus are as follows: Through the creation of a vacuum the vascularity of the part treated is so increased that penetration of the applied remedy actually occurs; the remedy, as well as the hyperemia, may repeatedly be reapplied to the same region; the medicinal substance is confined to the space covered by the cup used, minimizing dissipation in the atmosphere, and the remedial agent is delivered in an almost complete vapor form, also adding to the certainty of penetration. That the penetration really occurs and that the epidermal tissues retain the germicidal used for a considerable period of time have been repeatedly demonstrated in the clinics and research laboratories of The Skin and Cancer Hospital. Definite proof that these phenomena really occur will be submitted in another communication.

It is our belief, as the result of considerable experience, that this apparatus, with the germicidal agent used, constitutes a most useful treatment for epidermophytosis and epidermophytids as well as for tinea tonsurans, and marks a distinct advance over other local forms of therapy. Since the introduction of this treatment in the dermatologic clinic of The Skin and Cancer Hospital of Philadelphia, its use has extended to include the treatment for such pyogenic skin diseases as furunculosis, carbunculosis and some of the more resistant nonfollicular pyodermic infections.

Submitted for publication, July 17, 1931.

From the Research Laboratories and the Dermatologic Clinic of The Skin and Cancer Hospital of Philadelphia, Albert Strickler, M.D., Medical Director.

The essential parts of the apparatus are a pyrex retort (fig. 1 *A*) enclosed in an electrical unit (*B*) designed to produce the exact temperature necessary to generate the vapor. Vacuum is created by an inexpensive water pump attached to an ordinary water faucet. The water is turned on, and the vacuum is produced when the flow of water becomes rather silent. The produced vacuum is transmitted to the skin, and the vapor is carried through special vacuum cups, one of which is shown inserted in the throat of the retort (*A*). The apparatus is connected at *F* to a vacuum line by means of a rubber tube (*R*), and the vacuum thus created passes through the apparatus through

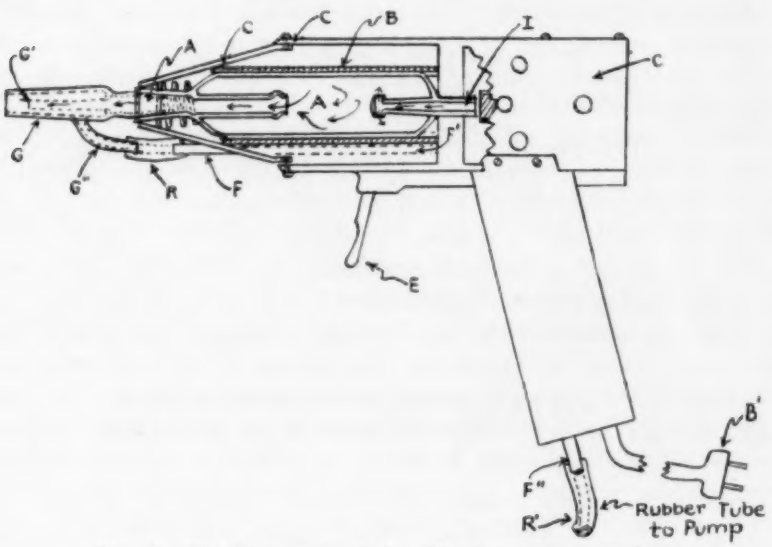

Fig. 1.—Working parts of the Henal vacuum vaporizer.

channels *F'* and *F''* and the tubing *R'*. The entire apparatus is enclosed in an aluminum casing.

The technic for using the Henal vacuum vaporizer is as follows: A measured amount of the medicinal powdered substance is poured into the retort through a glass funnel especially provided for that purpose. The electric cord, part of the electric heating system, is connected to an ordinary light circuit, and about ten minutes are allowed for the attainment of a maximum efficiency heat. The vacuum pump is then started. The mouth of the vacuum cup (*G*) is placed against the skin, and the air inlet (*I*) is closed by pressing the trigger (*E*). Vacuum is thus produced by the instrument and with it the desired hyperemic condition of that area of the skin is covered by the mouth of the cup. On releasing the trigger (*E*), the air inlet (*I*) is opened and the atmospheric pressure drives the vapor from the retort channel (*A*) through the

directing tube (*G*) and against the treated area. This procedure can be repeated on the same area as often as desired. Cups varying in design have been found best suited for treatment of various surfaces, as satisfactory creation of the vacuum depends on the snugness with which the cups are applied to the surface of the skin. It is most important to avoid air pockets between the margin of the cup and the surface of the skin. A set of five cups has been devised and found ample for treatment of any cutaneous surface.

In attaching the suction cup (*G*), the grinding is first slipped into the throat of the retort (*A*). Care should be exercised not to use too much force, for if the cup becomes jammed, considerable difficulty will be experienced when it is desirable to change the cups. Each of these cups has a slim tube (*G″*) which connects with a piece of rubber tubing (*R*). The other end of the rubber tubing (*R*) is connected to a

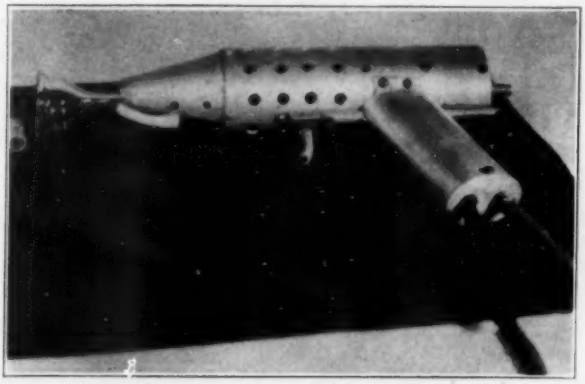

Fig. 2.—The Henal vacuum vaporizer, showing the funnel and measure for filling.

slim tube (*F*) that is part of the vacuum system. It is necessary to exercise a little care when connecting *G″* to *R*. When the apparatus becomes too hot, it is urgent to disconnect the current for a few minutes, and then restore the circuit. The presence of an excessive amount of crystalline substance on the skin indicates that there is too great heat, but lack of vapor shows insufficient heat. The apparatus may be refilled at any time, but when it is recharged while hot, it is best to rotate the instrument for a few minutes to insure even distribution of the powder in the retort.

CARE OF THE HENAL VACUUM VAPORIZER

After giving a number of treatments, the operator will notice that the rubber tubing connecting the pump with the instrument has lost its softness and elasticity. This is due to a coating on the inside of

the rubber tubing, the result of condensation of excess vapor drawn toward the pump. If this process is permitted to continue, it will eventually close the tube and prevent the production of a vacuum within the applied suction cup. It is necessary from time to time to renew

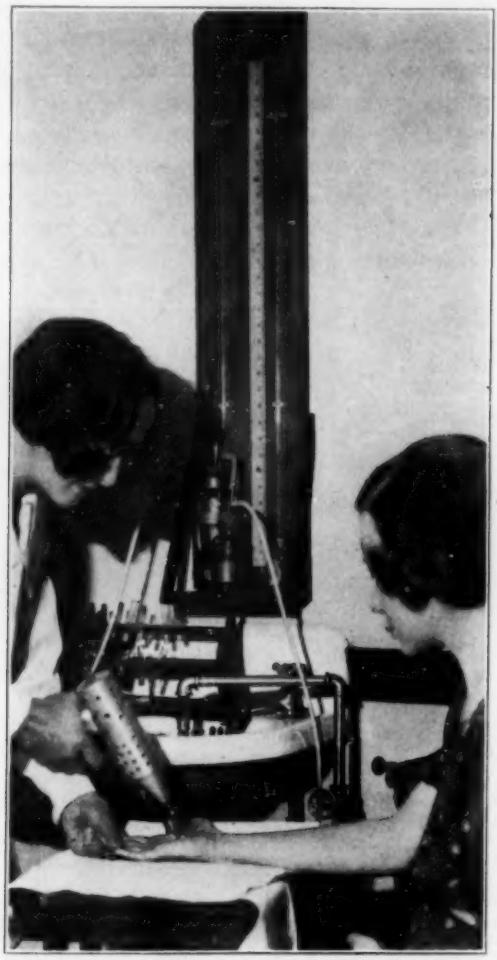

Fig. 3.—The complete outfit in operation. Note the rack of assorted cups, the vacuum mercury gage for measuring the degree of vacuum and the water faucet attachment necessary for obtaining the water pressure.

the rubber tubing. In order to lengthen the life of this tubing and keep the air channels clear, it is necessary to rinse or clean the instrument once daily, provided a large number of treatments have been given.

The rinsing or cleaning is done by connecting a small section of rubber tubing (about 12 inches [30.48 cm.]) to the front part of the instrument at *R*. The open end of this tube is submerged in a cup of alcohol. The trigger (*E*) is pulled back, as when a vacuum is being created. This will draw the alcohol through the instrument and down through the vacuum tube. To conserve the amount of alcohol used, it is suggested simply to dip the tube into the alcohol for a few seconds and then withdraw it. This is repeated a few times. A small amount of alcohol going through at intervals tends to dissolve the deposit within the rubber tubing more efficiently. After the alcohol, lukewarm water is used in the same manner, for the last rinsing. The 12 inch rubber tubing is then removed. It is used only for cleansing the instrument.

The same condensation that takes place within the lumen of the rubber tubing also forms in the interior of the suction cups, but it is even heavier, owing to the fact that the applicators are of lower temperature than the vapor. It is absolutely essential to cleanse the cups after every treatment, and after every application when exudate of pus or serum is present and finds its way into the cup. When serum, pus, blood or epithelial débris clings to the applicating cup, it must first be removed with cotton swabs saturated in water. The cup is then soaked in an alcohol bath, rinsed with warm water and allowed to dry. It is then again ready for use.

NOTE.—An electric driven vacuum pump has been devised and forms a unit of the Henal vacuum vaporizer. Its advantage is that it can be moved from one place to another and even taken to a patient's home.

"The Henal Vacuum Vaporizer" is to be distributed by the George P. Pilling & Son Company, Twenty-Third and Arch Streets, Philadelphia.

327 South Sixteenth Street.

Clinical Note

A MACHINE FOR MERCURIAL INUNCTIONS

OTTO LOWY, M.D., NEWARK, N. J.

In many instances a syphilitic patient discontinues treatment because of a distaste for the mode of treatment. For that reason, I have devised a machine to be used in the giving of mercurial inunctions to those to whom intramuscular injections are painful.

The diagram is self-explanatory. Pads of various sizes may be used. The forearms and thighs are treated alternately, and the patient soon learns to use

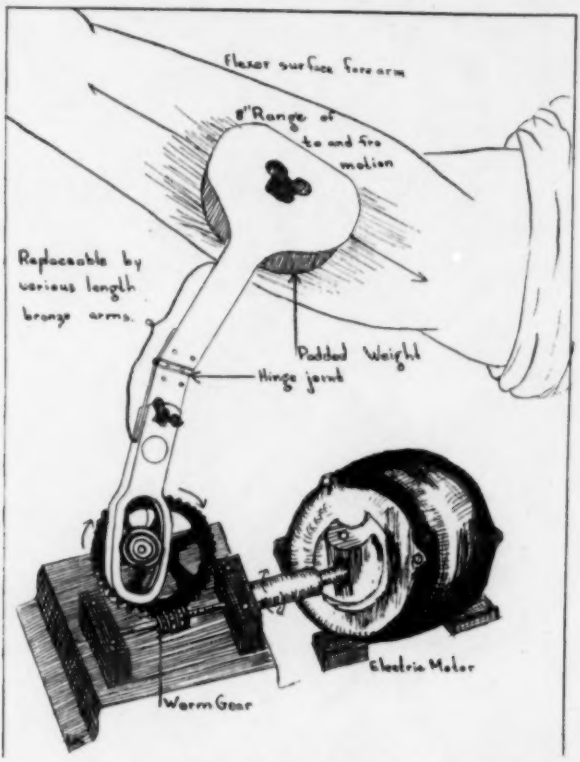

Diagram showing machine for the administration of mercurial inunctions.

the machine himself. He takes two or more treatments a week and times them himself. The amount of mercury used may be regulated by the physician or nurse. Those who rebel at injections of bismuth or mercurials are subdued by the promise of painless therapy.

I have used this method for five years, during which I have seen no cases of mercurial dermatitis. I am sure that I have retained under surveillance many patients who would have joined the horde of inadequately treated patients, because of the distaste for inunction at home, the pain of intramuscular injection or the fear of intravenous treatment.

I do not advocate the use of mercury to the exclusion of the arsenicals, bismuth or iodides.

Submitted for publication, Jan. 22, 1932.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

SOME ESSENTIAL FACTORS IN THE PATHOLOGY AND TREATMENT OF CANCER OF THE SKIN. LOUIS H. JORSTAD, Am. J. Cancer **16**:177 (Jan.) 1932.

The author recommends revision of the classification of epitheliomas of the skin into the following five groups: (1) typical basal cell carcinomas, in which the basement layer of cells undergoes division, but in which the basement membrane remains intact and in which metastases do not occur; (2) cystic basal cell carcinomas, characteristically multiple tumors; (3) adenoid basal cell carcinomas, a metastasizing and more malignant type closely allied to epitheliomas of the hair follicles, sweat glands and mucous glands; (4) basosquamous cell carcinomas, and (5) squamous cell carcinomas.

Jorstad states that carcinomas developing from keratoses may be either of the basal cell or of the squamous cell type, depending on the degree of keratinization. He favors treating all carcinomas of the skin as malignant, because of the difficulty of differentiating the various types on clinical considerations alone.

The *American Journal of Cancer* uses the word carcinomata in its text, and the reviewer has substituted the simplified nomenclature advocated by the American Medical Association Press.

DOES RADIATION CAUSE METASTASIS? EDITORIAL, Am. J. Cancer **16**:214 (Jan.) 1932.

There is no real clinical or experimental evidence that radiation destroys tumor cells. The impression that metastatic malignant conditions may occur more frequently following radiation than surgical intervention is attributed to the prolongation of life following radiation treatment, permitting time for the development of previously disseminated cancer cells into active malignant lesions.

THE STUDY OF SYPHILIS IN THE ETIOLOGY OF UVEITIS. PAUL O'LEARY, Am. J. Ophth. **15**:24 (Jan.) 1932.

An investigation of 354 cases of uveitis observed at the Mayo Clinic showed that 5.9 per cent showed clinical or serologic manifestations of syphilis. Clinical evidence of syphilis was present in more than 5 per cent of all patients admitted. O'Leary is careful to point out that the coexistence of uveitis and syphilis in these patients was not an implication that the uveitis was necessarily syphilitic. Antisyphilitic treatment resulted in material improvement in 33 per cent of the patients with uveitis and in slight benefit in 28 per cent. It is pointed out that ocular syphilis is resistant to treatment and that nonspecific benefit following antisyphilitic treatment may be obtained in definitely nonsyphilitic cases of uveitis. This latter observation applied to 42 per cent of the cases, while benefit followed antisyphilitic treatment in 62 per cent of the cases presenting syphilis and uveitis.

H. R. FOERSTER, Milwaukee.

ULCUS VULVAE ACUTUM ASSOCIATED WITH LESIONS OF THE MOUTH. MAX S. WIEN and MINNIE OBOLER PERLSTEIN, J. A. M. A. **98**:461 (Feb. 6) 1932.

The case reported is that of a girl of 17 years who had chronic recurrent painful ulcers on the mucous membrane of the mouth and of the vulva. She was undernourished, highly emotional and neurotic, and had a functional disturbance of the genital apparatus with amenorrhea whenever vulvar lesions existed. The oral lesions always preceded the occurrence of vulvar lesions by at least two

weeks, and at times oral lesions only occurred. The clinical similarity of these lesions with those of periadenitis mucosa necrotica recurrens (Sutton) and of the vulvar lesions with those of ulcus vulvae actum (Lifschütz) is discussed. The authors obtained pure cultures of B. crassus from the vulvar lesions at all times, and also from the vaginal secretion in the absence of genital ulcers. But at no time were these organisms present in the oral lesions. The writers believe that B. crassus is not the etiologic organism of ulcus vulvae acutum, but that it is a secondary invader on ulcers caused by endogenous factors.

The literature on the associated combination of oral and vulvar lesions is reviewed, together with a discussion of the etiology and pathogenesis, especially as to the possible relationship of the two conditions. The authors conclude that periadenitis mucosa necrotica recurrens and ulcus vulvae acutum are related conditions occurring on different sites but dependent on the same constitutional factors for their genesis, namely, the physical condition of the patient, nervous instability and endocrine imbalance.

AUTHORS' ABSTRACT.

PRACTICAL SOCIAL SERVICE IN A SYPHILIS CLINIC. E. NINNIS, J. Social Hyg. **18**:70 (Feb.) 1932.

This is a very readable article on the use of social service in the syphilis clinic of Stanford University Medical School. The reaching of sources of infection, prenatal care of syphilitic women, cost of treatment and follow-up forms are given consideration.

ANDERSON, Los Angeles.

TREATMENT OF ERYSIPELAS BY INJECTIONS OF MILK. I. A. SAYED, Brit. M. J. **1**: 281 (Feb. 13) 1932.

Excellent results were obtained in thirteen cases of erysipelas in which treatment by this method was given. Fresh milk is kept at boiling point for four minutes. It is then cooled and strained through gauze. From 5 to 15 cc. is injected as far as possible intradermally, the remainder subcutaneously. The injections are made parallel with and about 1½ inches (3.8 cm.) from the spreading margin of the lesion, the milk being injected at intervals along the line. In only one case did the infection spread beyond the site of injection. Of the thirteen patients treated, the disease in three was of the facial type; these patients were treated by means of intramuscular injections, with results as good as when the injections were made intradermally.

RATTNER, Chicago.

POIKILODERMA ATROPHICANS VASCULARE AND PARAPSORIASIS LICHENOIDES. FERNET, MORNET AND ODINET, Bull. Soc. franç. de dermat. et syph. **38**: 1438 (Dec.) 1931.

A man, aged 42, had a condition of the skin that had been slowly extending for twenty years without subjective symptoms. At the time of examination he presented a large plaque on the right lower side of the abdomen. Its surface was reddened, slightly atrophic and covered with fine adherent scales. At the borders of this plaque were noted lesions of a different aspect, consisting of small, round, rosy, lichenoid, slightly scaling papules, together with small punctate areas of atrophy and little networks of telangiectasia. On further search, identical lesions were found in other localities. The large plaque made a diagnosis of parapsoriasis in plaques seem plausible, but the other lesions bore all the earmarks of poikiloderma atrophicans vasculare. A biopsy gave no help. A possible relationship between these two disorders has been discussed before. Certain authors, including Civatte, believe that parapsoriasis lichenoides (or parapsoriasis variegata) is simply an incomplete form of poikiloderma atrophicans vasculare, while Brocq thought that there exists a transition form between parapsoriasis variegata and

parapsoriasis in plaques, which would explain the different lesions seen in this patient. In the discussion, Gougerot observed that the two diseases, poikiloderma atrophicans vasculare and parapsoriasis in its various aspects, may both appear in atypical forms and resemble each other closely.

ALOPECIA OF THYROID ORIGIN. A. SÉZARY and P. LEFÈVRA, Bull. Soc. franç. de dermat. et syph. **38**:1443 (Dec.) 1931.

General alopecia in a patient who had hyperthyroidism was cured by irradiation of the thyroid gland.

GOLD TATTOO. GOUGEROT, P. BLUM and C. DESGREZ, Bull. Soc. franç. de dermat. et syph. **38**:1462 (Dec.) 1931.

A case of chrysoderma, analogous to the one reported by Schamberg, is here put on record. The patient was a young man who was receiving gold sodium thiosulphate intravenously for pulmonary tuberculosis. Bluish-black staining developed in the bend of the right elbow, surrounding the site of injection. Chemical analysis of a piece of skin from the area of involvement resulted in a positive reaction for gold. The condition was reproduced experimentally by these authors in the skin of a rabbit by means of intradermal injection of gold sodium thiosulphate.

A CASE OF GENERALIZED ERYSIPELOID. P. CHEVALLIER, P. COLIN, M. LÉVY-BRÜHL, R. MORICARD and Z. ELY, Bull. Soc. franç. de dermat. et syph. **38**:1477 (Dec.) 1931.

A case of generalized erysipeloid is reported, accompanied by eight full page cuts. The authors state that the transmission of swine erysipelas to man is little known in France, and that the generalized form is of extreme rarity.

LICHEN PLANUS. GOUIN, BIENVENUE, DAOULAS and DESAUNAY, Bull. Soc. franç. de dermat. et syph. **38**:1497 (Dec.) 1931.

From a study of eleven cases it is concluded that lichen planus is intimately related to syphilis. The following arguments are advanced in support of this thesis: (1) the actual or probable existence of syphilis in the antecedents of nearly all the patients; (2) the known frequence of lichen planus in syphilitic persons; (3) the syphiloid aspect of certain lesions of lichen planus; (4) the therapeutic effect of antisyphilitic remedies on lichen planus; (5) the behavior of lichen planus under treatment with antisyphilitic drugs (Herxheimer reactions, reactivations, resistances, recidives), and (6) the negative serologic reaction in lichen planus, but the positive leukocyte reaction.

GANDY, Houston, Texas.

INFLUENCE OF POTASSIUM ON PRURITUS. J. SAUER, Deutsches Arch. f. klin. Med. **172**:219 (Dec. 21) 1931.

Sauer points out that although the sodium and calcium ions have been thoroughly investigated, little is as yet known about the therapeutic and physiologic action of the potassium ion. How he came to study the therapeutic action of the potassium ion is illustrated in the clinical history of a woman who had severe pruritus and occasionally urticaria. Influence of warmth made the pruritus more intense, and for this reason the patient suffered most severely at night. This factor was considered indicative of a hypersensitivity of the sympathetic nervous system and the itching was designated as "sympathetic pruritus." Since various therapeutic measures, such as diets free from sodium chloride and deficient in protein, or acid or alkaline diets, or the application of epinephrine or calcium chloride urea were ineffective, sodium bicarbonate was tried, but this likewise was ineffective. However, when potassium bicarbonate was given, a considerable

improvement was noted. In order to determine whether the efficacy was due to the potassium ion, potassium acetate was administered, and on the following day the pruritus had almost completely disappeared. Because of this favorable result the author employed the potassium therapy also in other cases of sympathetic pruritus. Patients with chronic lichen urticatus, in whom ointments and irradiations had proved ineffective, were given three times daily a tablespoonful of liquor potassii acetici, 30 cc., and aqua destillata, sufficient to make 200 cc. After two days the pruritus had disappeared but the skin eruption was not changed, and after eight days a gradual improvement became noticeable; yet after two weeks it appeared as if there was no further progress in the curative process, and the pruritus recurred temporarily. In order to reactivate the potassium action, calcium lactate was given for one day and as a result of this the pruritus and eczema showed an exacerbation, but when potassium acetate was given once more the healing progressed further. Of nine patients with lichen urticatus, only two were refractory to the potassium therapy and both of them were men. In women the treatment was much more effective. Several cases of chronic eczema of the hands likewise yielded to potassium therapy. [J. A. M. A.]

THE DIAGNOSTIC VALUE OF REPEATED REACTIONS TO TUBERCULIN IN TUBERCULOSIS OF THE SKIN. HEINRICH REISS, Dermat. Wchnschr. **94**:93 (Jan. 16) 1932.

An intracutaneous injection of 0.1 cc. of Koch's old tuberculin was given in a dilution of 1:10,000. The reaction was measured after forty-eight hours. In one week the injection was repeated in the same location. Equal reactions, according to Bessau, speak for active tuberculosis, an increase in the second reaction for inactive tuberculosis and a decrease in the second reaction for active or inactive tuberculosis in a cachectic person. The author followed this technic in 203 cases with the following results:

Table of Reaction

Diagnosis	Active, Per Cent	Inactive, Per Cent	Cachectic, Per Cent	Negative, Per Cent
No clinical tuberculosis	10	43	37	10
Inactive tuberculosis of the chest	0	53	37	10
Manifest skin tuberculosis	50	21	29	0
Lupus erythematosus	7.7	69.3	23	0

ECZEMA IN AN AREA OF HYPESTHESIA. E. SCHRÖPL, Dermat. Wchnschr. **94**:103 (Jan. 16) 1932.

A patient had ulnar paralysis of the left forearm following an injury. Eczema developed as a result of chemicals encountered in his work. It remained limited to the area of hypesthesia for six years.

PSEUDO-ANTHRAX IN MAN. TONKA TONEWA, Dermat. Wchnschr. **94**:133 (Jan. 23) 1932.

A bullous eruption with a marked inflammatory reaction developed on the right hand of a woman aged 26. She had milked a cow suffering from cowpox on the udders. Clinically, the condition resembled "milker's nodes," except that the inflammatory reaction suggested anthrax. Cultures from the lesions showed an anthrax-like organism, which, however, liquefied gelatin and formed spores in bouillon. Further bacteriologic study identified the organism as Bacillus pseudo-anthracis, which is usually nonpathogenic. The conclusion reached was that a "milker's node" had developed which was a good culture medium for the pseudo-anthrax bacillus.

THE TREATMENT OF RARE FORMS OF ORIENTAL BOIL. HOULOUSSI BEHDJET, Dermat. Wchnschr. **94**:138 (Jan. 23) 1932.

The author describes a number of unusual cases of oriental boil in which the lesions resembled tuberculosis of the skin and hemangiomas, in which the diagnosis could be proved only by finding the organism. He has had the best results by destroying the lesions with diathermy.

THE TREATMENT OF ANGIONEUROSIS DOLOROSA FOLLOWING ARSPHENAMINE THERAPY. KLAUS DREYER, Dermat. Wchnschr. **94**:142 (Jan. 23) 1932.

A painful angioneurotic spasm developed in a patient following the eighth injection of sodium arsphenamine, and recurred with more severity following the next injection. Infra-red irradiation during succeeding injections prevented a recurrence of the symptoms.

TOPHI ALONE AND IN COMBINATION WITH SYPHILIS AND VARIOUS CUTANEOUS CHANGES. A. JORDAN, SCHAMSCHIN and DOBROW, Dermat. Wchnschr. **94**:161 (Jan. 30) 1932.

The authors briefly review the literature in regard to the frequency of cutaneous changes in connection with gout. They report the cases of three patients with numerous tophi, one of whom showed accompanying changes in the nails and the other two a more or less generalized eruption. Of the two with cutaneous eruptions, one had a positive Wassermann reaction and the other a dilated aortic arch, but in neither was the eruption influenced by antisyphilitic therapy.

CAN AN INJECTION OF DIPHTHERIA SERUM CALL FORTH A POSITIVE SERO-REACTION IN A NONSYPHILITIC PERSON? HARALD BOAS and GUDRUN TÖLBÖLL, Dermat. Wchnschr. **94**:173 (Jan. 30) 1932.

In 100 patients with diphtheria, Wassermann and Kahn tests were performed before and after serum treatment. In one instance a positive reaction occurred one week after treatment, but it had cleared entirely six days later.

EXPERIMENTAL INVESTIGATIONS OF THE CUTANEOUS CHANGES IN EXTERNAL AND INTERNAL CHRONIC THALLIUM POISONING. A. BUSCHKE and J. VON VÁSÁRHELYI, Dermat. Ztschr. **63**:37 (Jan.) 1932.

As a result of experiments carried out on rats, mice and monkeys, the authors show that local applications of thallium cause generalized alopecia and slight inflammatory changes similar to those caused by the internal administration of the drug. Local alopecia appears before the generalized falling out of the hair when the thallium is applied locally. The action of the drug is explained on the basis of the effect on the nerve endings.

PSORIASIFORM ARSPHENAMINE EXANTHEM. E. ZURHELLE, Dermat. Ztschr. **63**:41 (Jan.) 1932.

Mild arsphenamine dermatitis developed in a patient with chronic psoriasis while being treated for syphilis with neoarsphenamine. An exacerbation of the psoriasis occurred, and histologic examination showed psoriatic lesions developing on the basis of a dermatitis.

EXPERIMENTAL NICKEL DERMATITIS. WILHELM MILBRADT, Dermat. Ztschr. **63**:47 (Jan.) 1932.

Repeated painting of the ears of white mice with 20 per cent nickel sulphate solution resulted in a typical dermatitis in 90 per cent of the animals in between three and five weeks. The use of a 1 per cent solution gave no results. After

painting with the 20 per cent solution for long periods, from two to four months, a specific desensitization occurred. The inflammatory reaction was a local allergic manifestation, no evidence of a general allergy developing.

EXPERIMENTS WITH CISTERNAL INOCULATIONS OF SYPHILIS INTO RABBITS. GISELA SCHULTZE-WOLTERS, Dermat. Ztschr. **63**:57 (Jan.) 1932.

The author injected chancre emulsion rich in spirochetes into eight rabbits by cistern puncture. As a control, 0.85 per cent sodium chloride was similarly injected into two rabbits. Fluid obtained seventy hours later showed living spirochetes in two instances, though in rather small numbers. All of the animals injected with the chancre emulsion showed signs of meningeal irritation, which did not occur in the case of the control animals.

ENDOPHLEBITIS SYPHILITICA AS AN INDIVIDUAL CLINICAL ENTITY. WILHELM RICHTER, Dermat. Ztschr. **63**:63 (Jan.) 1932.

The patient presented bluish-red papules on his feet, arranged in a more or less linear manner. The Wassermann reaction of the blood was positive, and the lesions cleared up under antisyphilitic therapy. Histologically, the pathologic changes were limited to the veins. Subsequently, a gangrenous ulcer developed on one toe, requiring amputation. This was apparently due to changes in the venous system affecting the capillaries.

THE RAPID DIAGNOSIS OF MALARIA BY MEANS OF THE DARK FIELD. A. WOLTER, Dermat. Ztschr. **63**:68 (Jan.) 1932.

Wolter points out the ease with which the malaria organism may be seen by dark-field illumination, either unstained or stained with 1 per cent alcoholic solution of methylene blue, neutral red or brilliant cresyl blue.

TAUSSIG, San Francisco.

THE SKIN AS A PROTECTOR AGAINST LIGHT. HANS MEYER and H. KIRCHHOFF, Deutsche med. Wchnschr. **58**:41 (Jan. 8) 1932.

The skin has two protective mechanisms against excessive ultraviolet irradiation. The short waves of the ultraviolet ray are filtered by the layer of keratin; after excessive treatment by light hyperkeratosis occurs. The longer waves of the ultraviolet rays are filtered by the melanin of the cutis. Melanin has an important rôle as the regulator of the heart rays also. The absorption of ultraviolet rays by different concentrations of melanin solution is demonstrated in the original article by curves. Colorless protein solution has only half as much absorbing power as melanin. When the colorless protein is converted to melanin, the power of absorption is increased. This protective mechanism of the skin against excessive penetration of ultraviolet rays indicates that the good effect of the rays is limited to a certain dosage.

MILK-FREE DIET OF INFANTS SUFFERING FROM ECZEMA. R. HESS, Deutsche med. Wchnschr. **58**:52 (Jan. 8) 1932.

Infants suffering from eczema can be fed satisfactorily without milk. Hess advised the use of almond milk in 6 to 10 per cent solution, with the addition of carbohydrates. He has also obtained good results with a whey preparation. Although these feedings can be kept up for months with good results, they should be considered as transitory. Under this regimen the eczema showed definite improvement.

KERESZTURI, New York. [AM. J. DIS. CHILD.]

CHRONIC ECZEMA AND CATARACT: REPORT OF A CASE. G. LEVY, Klin. Monatsbl. f. Augenh. **86**:681 (May) 1931.

A man, aged 23, had suffered from many attacks of eczema since his sixth year of life. After a free interval of two years, the eczema had recently returned. Simultaneously the left eye presented an advanced cataract, and the right eye, subcapsular opacities, somewhat star-shaped in the posterior cortical, a few dotted opacities in the nucleus and a few opacities in the vitreous. A connection is seen by the author between the cataracts and the eczema, which may be termed neurodermatitis in this case, both being caused by endocrine dysfunction. The evolutionary relationship between lens and skin seems to suggest that the same endocrine dysfunction would manifest itself as eczema in the skin and as cataract in the lens. Publications in point by Rothermund, Andogsky, Loewenstein, Vogt and Kurz are referred to.

K. L. STOLL [ARCH. OPHTH.]

CHRONIC THYROID INSUFFICIENCY IN AN ADULT. EMIL PETRÁČEK, Česká dermat. **12**:233 (April) 1931.

The case reported substantiates the theory (Samberger-Eppinger) that the thyroid hormone is essential to the maintenance of normal tonus of the blood vessels and lymphatics.

In a man, aged 54, who had a generalized dermatitis of several months' duration, a solid edema developed on the face and extremities, with vesicles, bullae and profusely weeping areas. Most of the hair fell out; the remaining hair was dry, dull and brittle. The secretion of sweat and sebum was entirely arrested. The nails were dry and deformed; the tongue was swollen. The patient was apathetic and disoriented and suffered from hallucinations. The basal metabolic rate varied from low normal to minus 12. Sugar tolerance was increased. The thyroid was normal on palpation. The patient responded promptly to thyroid therapy.

The foregoing clinical picture is not one of pure myxedema, but shows an edema from venous stasis combined with lymph stasis. The latter is evidenced by the presence of vesicles, protracted weeping and biopsy, which showed lymphangiectasis and an increase in connective tissue bundles. In discussing the etiology, the author reasons that the generalized dermatitis damaging an enormous number of capillaries of the skin through inflammatory changes put in an excessive demand for thyroid hormone and led to exhaustion of the thyroid. The gland may have been below par (congenital or acquired hypofunction) and further affected by senile and arteriosclerotic changes.

SPINKA, Texarkana, Texas.

PREVIOUSLY UNDESCRIBED FORM OF ANURESIS IN A BURN. MARIE RUNTOVÁ, Česká dermat. **12**:242 (April) 1931.

The author reports a case of extensive second and third degree burns, the deepest gangrenous lesion involving the lumbosacral region, which led to functional paralytic ileus and retention of urine lasting five weeks, to the patient's death. She believes that the burn involved, through the posterior sacral foramina, the roots of the third and fourth sacral nerves, which supply the sphincter ani, the sphincter vesical and the detrusor urinae.

SPINKA, Texarkana, Texas.

MODERN FROST-BITES. K. H. KOVANIC, Česká dermat. **12**:257 (May) 1931.

Fashionable dress accessories bring new types and new locations for frost-bites:

Linear dermatitis, sharply demarcated and covered with vesicles, extending from the supraclavicular notch down for 6 cm., was caused by contact with the metal part of a "zipper" jacket fastener." Metal "zipper" fasteners on high galoshes brought on symmetrical linear dermatitis in two cases. Mechanical constriction and friction were contributory causes. The wearing of galoshes over stocking feet caused frost-bitten toes and frost-bite of the medial plantar region in a woman

with hyperhidrosis and pes planus. A linear, semicircular dermatitis over the back of the neck resulted from the rubbing of a steel helmet that a gendarme pushed off his perspiring forehead while on a winter march.

SPINKA, Texarkana, Texas.

IMPORTANCE OF SECONDARY INFECTION IN LUPUS VULGARIS. S. PAVLOV, Sov. Vest. dermat. **9**:567 (Sept.-Oct.) 1931.

The author had under observation for three years a case of an ulcerative, vegetative disease of the skin of the face and back that started with a deep pustule. Inoculation into guinea-pigs was positive for tuberculosis, and cultures made from the pus revealed Staphylococcus aureus. Because of the great obstinacy of the condition to treatment with pyrogallol and to the roentgen rays, the author tried staphylococcus autovaccine, which caused the ulcer to heal rapidly and to reveal a typical flat lupus vulgaris.

The author believes that many cases of atypical chronic tuberculosis described in the literature under different names (chronic purulent tuberculosis, Jadassohn, lupus congestive, Brocq, tuberculosis luposa exudativa, Podwyssotzkaya) are similar cases of mixed infection.

SPORADIC CASES OF PELLAGRA IN NORTHERN RUSSIA. D. S. GINZBURG, Sov. Vest. dermat. **9**:575 (Sept.-Oct.) 1931.

From 1926 to 1930, the author observed five cases of pellagra, all in women from 22 to 62 years of age, one a city dweller, the others peasants. Not only the exposed parts of the skin were involved, but also the thighs, the genitals and the anal region. Two cases that ended fatally presented a clinical picture of pellagrous typhus with a normal temperature. The author concludes that pellagra is of infectious etiology, and that sun rays play only a limited rôle in its causation.

CHANGES IN THE NERVES OF THE SKIN IN DIFFERENT SKIN DISEASES. M. A. ROSENTUL, Sov. Vest. dermat. **9**:585 (Sept.-Oct.) 1931.

The author has examined the nerve fibers of the skin by the silver method of Bielschowsky in healthy and diseased skin (Recklinghausen's disease, eczema, prurigo ferox Hebra, lupus vulgaris, tuberculosis verrucosa cutis, radiodermatitis and kraurosis vulvae). He considers the methods of Golgi, Dogel, Rachmanoff and Schultze as too complicated and as yielding unsatisfactory results.

He found free nerve endings in the hair but only in the outer hair sheath. Around the sebaceous glands there were a great number of medullated and non-medullated fibers, but no nerve fibers were found in the glands themselves. Swellings of the axis-cylinder were observed at the beginning of demyelinization of nerve fibers, and later mufflike swellings were seen in places of the Schmidt-Lantermann incisures, the nerve assuming the appearance of a row of eights lying horizontally close to each other. Between the constrictions of Ranvier were naked axis-cylinders. Irregular impregnation of the nerve with silver is not accidental, but due to a chemically changed nerve fiber.

The changes in the nerves of the skin in inflammatory processes were quite different from those in atrophy or proliferation. In the former the changes were analogous with those in neuritis; in atrophy there was degeneration, and in proliferative processes of the skin there were degenerative and also regenerative changes in the nerves. This explains the restitution of the fiber in the healed skin.

ERYTHRODERMIAS. E. D. DANILEVSKAYA, Sov. Vest. dermat. **9**:591 (Sept.-Oct.) 1931.

The author studied twenty-three cases of erythrodermia during the last twelve years, and came to the following conclusions: Cases of secondary erythrodermia are much more frequent than primary cases. Their number increases from year to

year. Men are more frequently affected than women. The patients are between 35 and 55 years of age. White dermographism is a constant sign of the first period of the disease; at the height of the dermatosis dermographism is absent, and during the period of convalescence there is a normal vascular reaction. In erythrodermias associated with pruritus, enlarged glands are found, particularly in the inguinal and femoral regions. Improvement in the dermatosis parallels the decrease in the size of the glands and vice versa.

PECULIARITIES IN THE SERODIAGNOSIS OF PREGNANT WOMEN. S. A. TSHUGUIEV and I. M. KOVALSKI, Sov. Vest. dermat. **9**:601 (Sept.-Oct.) 1931.

Investigation of the Wassermann reaction of the blood of pregnant women revealed an unspecific reaction in 5 per cent of the cases when syphilitic antigen was used and in 3.6 per cent when complex antigen was used. The author advises, therefore, the use of an unspecific cholesterolized antigen in the dilution of 1:1,000 or 1,200, which does not give an unspecific reaction.

TREATMENT OF BURNS WITH DRY HOT AIR. P. K. KARPOV, Sov. Vest. dermat. **9**: 605 (Sept.-Oct.) 1931.

The author for experimental purposes produced burns on his skin and on that of a nurse, and used dry hot air in treatment. His observations brought the following conclusions: Dry hot air applied to a burn diminishes the amount of exudation. When this treatment was applied immediately to burns that were produced by temperatures causing burns of second to third degree (according to Behrend, second degree burns are produced with from 75 to 100 degrees of temperature), the formation of bullae was not prevented, but their size and number were limited, and pain was lessened. Further treatment with heat brought about quick healing even when no other kind of treatment was used. Burns produced by lower temperatures, which cause burns of second to first degree, could be aborted by one application of dry warm air; no blisters formed and no further treatment was necessary. First degree burns were, of course, favorably influenced in regard to pain and rapid healing.

TREATMENT OF CUTANEOUS STAPHYLOCOCCIC AND STREPTOCOCCIC INFECTIONS BY MEANS OF FILTRATES OF BESREDKA. E. V. KISTIAKOVSKY, Sov. Vest. dermat. **9**:615 (Sept.-Oct.) 1931.

From a review of the literature and from his own experience the author comes to the conclusion that Besredka filtrates used in the form of compresses are a specific remedy for erysipelas and superficial staphylococcic infections. In the latter and in sycosis, intracutaneous administration is also very useful. In the majority of cases this injection gives a strong local as well as a general reaction. Therefore, the initial dose should not exceed from 0.1 to 0.3 cc. The staphylococcic filtrate is more toxic than the streptococcus filtrate, because it contains a greater amount of toxin. Although the effect of the filtrates is due to the bacterial toxins, there is no doubt that the toxins produced in the local foci by the inflammatory reaction also play a rôle.

FEVER IN SYPHILIS. E. S. ZALKIND, Sov. Vest. dermat. **9**:626 (Sept.-Oct.) 1931.

The author describes two cases of fever in syphilis. One occurred in a man with recent syphilis, who had suffered for four months with slight fever, asthenia, loss of weight and general malaise. The other case was in a woman with an old syphilitic infection, who complained of high fever, chills and night sweats. She had an enlarged spleen and liver. In both cases the Wassermann reaction was positive, and bismuth therapy had a rapidly favorable effect.

BLOOM, New York.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

LEO SPIEGEL, M.D., *Secretary*

Regular Meeting, Dec. 1, 1931

JOSEPH J. ELLER, M.D., *Chairman*

ULCERATION OF THE WRIST. Presented by DR. JOSEPH J. ELLER for DR. NOVEKOFF.

P. K., a man, on Oct. 3, 1931, was bitten on the dorsal surface of the right forearm by an insect. The area became inflamed and swollen and progressively worse. On October 24, the patient was admitted to the Coney Island Hospital with a diagnosis of carbuncle. Examination of the lesion on the patient's admission showed a large, circumscribed, indurated, tender, erythematous area on the dorsal surface of the right forearm, fluctuating at the center, adherent to the underlying tissue and not painful. This area was incised and no pus was found. A section was removed for pathologic examination, and the patient was discharged.

On Nov. 11, 1931, the patient was readmitted to the hospital with a generalized erythematous nodular eruption, not tender or fluctuating and without subjective symptoms. The patient stated that the eruption appeared two weeks after his discharge from the hospital. At this time the original lesion had grown larger, was more indurated and tender, gaped widely and was painful and itched.

Laboratory Examination: On Oct. 3, 1931, the blood count showed 9,820 white cells, with 11 per cent lymphocytes and 79 per cent polymorphonuclears. Examination of the urine and the Wassermann test gave negative results. Biopsy showed chronic suppurative inflammatory reaction.

On readmission of the patient on Nov. 24, 1931, the blood count showed: white blood cells 7,500, with polymorphonuclears, 60 per cent; lymphocytes, 25 per cent, and transitionals, 15 per cent. The blood culture gave negative results. The Wassermann test was negative and also the results of urinalysis. Nasal culture was negative for B. leprae. Dark-field examination of serum from the lesions was negative for spirochetes. The report of the biopsy on the eruption and the lesion was not ready at the time of presentation.

The treatment was symptomatic.

DISCUSSION

DR. SIGMUND POLLITZER: I came to no definite conclusion regarding this case. The patient told me that the large ulcerating tumor on the forearm followed an insect bite, ten weeks ago, which awakened him from a sleep on the sand at the sea shore. He did not see the insect. The spot itched, and he scratched it. Within a few days there was considerable swelling, for which he saw a physician, who incised the tumor, which, however, continued to grow until it assumed its present appearance. Two months later the generalized lesions, now present, began to appear, first on the face, and within a fortnight fresh lesions were scattered widely over the integument.

The first question is, what relation, if any, exists between the tumor on the forearm and the general eruption? One can deal only in surmises until the nature of the tumor is known. Only biopsy can answer that question; if the tumor is a sarcoma — which is entirely possible — one would have to consider the probability of metastatic dissemination as the cause of the general eruption. These lesions, however, are soft, edematous and bright red — factors that speak against a diagnosis of disseminated sarcoma. Some of the lesions furthermore, have faded

away, leaving normal skin or slightly pigmented spots. The patient seems otherwise well; there is no systemic reaction. It is not out of the question that the generalized eruption has no etiologic connection with the lesion on the forearm and that it may be a drug eruption. To sum up my vague impressions, I should say that at present there are not sufficient data on which to base a diagnosis in this extraordinary case.

DR. CHARLES WOLF: My impression is that the primary tumor was on the forearm and by incising it the tumor metastasized very rapidly. A biopsy should help in clearing up the diagnosis. My tentative diagnosis is generalized sarcomatosis.

DR. C. GUY LANE (BOSTON): This case suggests one that I saw seven or eight years ago. In that case there was a much more extensive ulceration over the whole forearm, with exposure and involvement of the bones. There were also similar purplish, though somewhat firmer, nodules scattered over the body, in contrast to the softer nodules in the case presented here, which may be due to the fact that the latter are earlier lesions. The case that I saw was later proved by biopsy to be one of angiosarcoma.

DR. A. BENSON CANNON: If I had only the fungus lesion of the wrist to consider, I should have suggested mycosis fungoides. I do not know whether the secondary lesions, if they can be called such, on the body, fit in with a diagnosis of mycosis fungoides, but I think so. A number of years ago I saw a similar condition diagnosed as a carbuncle and incised. The diagnosis was then changed to a fungating epithelioma, and the true nature of the disease was not suspected until the develoment of multiple secondary tumors of the skin, a few weeks later. The course was rapid, and the patient died following a perforation of the abdominal wall from an ulcerating fungous mass. Like the other members of the Academy, of course, I think that it is impossible to make a definite diagnosis without a thorough study of the case with histologic examination of the tumors and fungous ulceration.

DR. MARION SULZBERGER: Clinically the picture presented is almost exactly like that of a case shown in Jacobi's Atlas under the title of sarcomatosis cutis. The color and distribution resemble this case so closely that I was immediately reminded of that picture. The lesions are probably due to metastases (and inflammatory reaction to metastases) from a primary small round cell sarcoma of the arm. This is the type of sarcoma with the most tendency to rapid metastasis.

DR. BOLESAW LAPOWSKI: The patient has: (1) red spots the size of a penny on the hard palate; (2) pigmented spots from absorption of the lesions on the legs, and (3) active, pulplike, soft, raised erythematous lesions on the body, which appeared one or two months after the lesion on the forearm was excised. There were no chills, headache, fever or any other subjective symptoms. There is no infiltration around the lesions. The patient has been taking medicaments internally before and after ulceration of the wrist. All these points suggest dermatitis medicamentosa or toxic eruption. The condition is neither a sarcoma nor mycosis fungoides. To my mind, the lesions on the body will be absorbed in the same way as the lesions on the legs, leaving pigmentation.

DR. HOWARD FOX: The two most likely possibilities in my opinion are mycosis fungoides "à tumeurs d'emblée" or a generalized lymphosarcoma.

DR. FRED WISE: My impression is that of primary sarcoma of the forearm, with metastases in the skin. I think that the distribution and color of the disseminated lesions are characteristic. The prognosis is poor.

DR. J. FRANK FRASER: Some of the points raised by Dr. Lapowski are very well taken, but, after all, the final diagnosis must rest on the histopathology. The report, as I understand it, does not give any evidence of a neoplastic process. If this were a generalized sarcomatosis, we should expect by this time to see some constitutional symptoms. There should be evidence of metastases in the internal organs. Dr. Lapowski mentioned that some of the lesions on the lower

extremities had undergone complete resolution, leaving pigmented scars. This fact speaks against sarcoma.

DR. LEO SPIEGEL: I do not know what the condition is, but the patient does not appear sick, there is no cachexia, and I agree with Dr. Lapowski's remarks that the condition may be due to a drug.

DR. JOSEPH J. ELLER: The chairman will report on the further microscopic studies in the case.

NOTE.—The patient died a few weeks after presentation. The histology of a skin lesion was suggestive of mycosis fungoides.

FOLLICULITIS; SCARS. Presented by DR. HERMAN GOODMAN.

P. K., a woman, aged 33, married, for five years had had numerous small scars on the flanks. These scars were preceded by pustules, which the patient denied picking. For one month there had been many pustules on the chest, flanks and arms. The family history was negative, as was the past history, except for frequent attacks of disturbance in the gallbladder. The marital history was normal. The urine and the results of chemical examination of the blood were normal. The Wassermann and Kahn reactions were negative.

Biopsies: A section from the follicular lesion showed an area of round cell infiltration scattered in the mid and lower corium. The upper corium showed a great amount of edema of the collagen fibers. The blood vessels were dilated but not especially engorged. The cellular exudate consisted of lymphocytes and a few connective tissue cells with very small nuclei.

A section from the scars showed a very edematous condition in the upper corium and in the mid corium. The epidermis was replaced by normal epithelium. The blood vessels were surrounded by a moderate amount of round cell infiltration, and the blood vessels around the hair follicles were engorged.

DISCUSSION

DR. HERMAN GOODMAN: The patient shows several types of lesions. The active lesions are said to have begun as small superficial infiltrations the size of a pea or smaller deep in the skin and without surface marking. The lesions raise the skin above them, and become compressible. The center undergoes necrosis, and a crust forms, which falls off leaving an ulcerated area. The scars are small, and give the impression of being raised, yet stretching the skin leads to flattening of the raised appearance. Sections from active lesions and from scars have been removed and sectioned. There are no active or definite pictures of tuberculosis or of tuberculid. The patient was shown last week at the clinical meeting of the Stuyvesant Square Hospital; the physicians present thought the diagnosis of pyoderma applicable to the eruption.

A CASE FOR DIAGNOSIS (PSORIASIS?). Presented by DR. HERMAN GOODMAN.

J. A., a boy, aged 9 years, was admitted to the Stuyvesant Square Hospital clinic on Sept. 22, 1931, because of dry, scaly, thickened, fissured areas on both palms. There were similar, more circumscribed patches on the soles and over both inner malleoli, and follicular keratotic lesions on the right elbow. These lesions were of two years' duration; they were worse in winter.

The family history was unimportant. The past history, aside from measles, whooping cough and frequent colds, revealed nothing of significance.

The urine was normal. Chemical examination of the blood showed 19.5 mg. of urea nitrogen, 2.22 mg. of uric acid, 103.2 mg. of sugar and 487.6 mg. of chlorides per hundred cubic centimeters. The trichophyton and the Wassermann tests were negative.

Biopsies: A specimen from the ankle showed hyperkeratosis. There were cellular infiltration of the dermal papillae and extravasation of blood into the stratum corneum.

A specimen from the right hypothenar eminence showed a very irregular epidermis with long thin rete pegs. Many suprapapillary plates were thin. There was round cell infiltration scattered through the epidermis as well as a suggestion of vesicle formation in places. There were edema and a round cell exudate in the papillary bodies. The blood vessels in the upper corium were dilated. The whole epidermis was covered by a thick nonparakeratotic scale.

DISCUSSION

DR. A. BENSON CANNON: I would follow the suggestion that Dr. Eller offered, that if he had to make a definite diagnosis it would be psoriasis. I know of no other condition that would give similar bilateral, symmetrical, sharply demarcated, dry red plaques with fissuring and mycaceous scales. Two of the fingernails showed stippling such as is seen in cases of psoriasis.

DR. HOWARD FOX: I think there are two possible diagnoses in this case, namely, psoriasis and dermatophytosis. The fact that the patches clear up in the summer would favor the diagnosis of psoriasis rather than of a fungus infection.

DR. HERMAN GOODMAN: It was my impression that clinically this child presented psoriasis of the palms and soles. It is difficult to make a diagnosis of psoriasis from such limited areas, which do not lend themselves to critical study for the appearance of the pellicle of Bulkely or of the bleeding points of Auspitz. The prepared section of skin is not characteristic of psoriasis, although typical clinical psoriasis does not always show typical histologic pictures. The second diagnosis is keratosis palmaris et plantaris.

An enlarged gland developed in the left axilla, and the patient was given generalized exposure to the ultraviolet radiation from the air cooled mercury vapor arc in quartz. The gland disappeared after two or three irradiations. The palms and soles were given added treatments with these rays, but the change was not lasting. It is difficult to clear psoriasis with artificial sunlight.

The patient shows fissuring of the tongue. The resemblance to scrotal tongue led Dr. Wise to express the thought that the diagnosis of keratosis palmaris et plantaris was to be favored. There are no relatives with a similar condition. The patient's parents were not blood relations.

GENERALIZED ERYTHRODERMA FROM BISMUTH IN A PATIENT WITH A FIXED TYPE OF LUPUS ERYTHEMATOSUS OF THE FACE. Presented by DR. E. WILLIAM ABRAMOWITZ.

J. D., a man, aged 42, born in the United States, was a fireman by trade, but for the past two years had been acting as a watchman. He was married and the father of five healthy children. He had never been seriously ill. Twenty years prior to presentation he had been severely injured through an explosion of a boiler and had received a fracture of the legs and injuries to the spine with severe burns on the body. The skin on the face, however, was only slightly involved. Shortly after this, he noticed an eruption appearing on his nose which had persisted during the period of eighteen years and had finally affected almost the entire face.

The patient presented himself at the New York Post-Graduate Skin Clinic on Oct. 30, 1931, with lesions covering the entire face above and below the eyes and extending to the ears, with a characteristic butterfly distribution on the nose and cheeks. The eruption consisted of patches that were markedly erythematous and scaly, with areas of atrophy, telangiectasis and dilated follicles. The scales were sharply adherent. On the back of the left ear was an erythematous and scaly area, the size of a half dollar, which was atrophic. The lower lip presented a marked degree of scaliness. The scalp was devoid of lesions. On the upper part of the back was a senile keratotic lesion the size of a pea. A biopsy specimen was taken from a scaly and indurated spot the size of a pea located just above the right eyebrow. This turned out to be a prickle cell epithelioma and was evidently

a secondary manifestation. It was decided to treat the patient with intramuscular injections of bismuth salicylate in oil and also with an ointment of bismuth applied to the affected skin of the face.

The patient noticed an eruption appearing immediately after the first injection of bismuth but never mentioned anything to the examining physician when he returned the following week for the second injection. Following the second injection, the eruption became generalized, involving the entire trunk and upper and lower extremities. It was most marked on the face and the exposed parts of the chest and hands. The gross appearance was that of a generalized erythematous dermatitis with fine scaling but no vesiculation. The general condition of the patient was good; there was no fever, enlargement of glands or stomatitis. The patient complained of severe itching. Injections and local medication were immediately discontinued, and a soothing lotion was prescribed. In addition to his present occupation of watchman, he had helped in unloading sand from scows and was unduly exposed to the sun.

As presented, the skin showed profuse redness and scaling with slight edema. The skin of the palms and soles was markedly thickened. There was no bismuth line present on the gums. The urine was normal and the Klein test was negative.

The interesting feature was that the patches of lupus erythematosus on the face were markedly improved since the appearance of the generalized dermatitis.

DISCUSSION

DR. BOLESLAW LAPOWSKI: For what purpose was bismuth used in this patient with lupus erythematosus?

DR. E. WILLIAM ABRAMOWITZ: In answer to Dr. Lapowski's question, injections of some form of bismuth are frequently of benefit in lupus erythematosus and should be given a trial in cases in which the patients do not respond to treatment with gold preparations. Like the latter form of treatment bismuth therapy is now a recognized form of treatment for this disease.

DR. A. BENSON CANNON: I think that eruptions of the skin caused by bismuth are so rare that this particular case should not be passed over without comment. I have seen but one case that I thought could be ascribed to bismuth and that was not a universal eruption, but only a mottled, localized erythema. I did see two cases in 1924 shown by Dr. Oppenheim in Vienna, in which there was generalized erythema, rather of a scarlatina type, with no vesiculation following injections of bismuth. I think that if one takes into consideration the enormous amount of bismuth used and the infrequency with which cutaneous lesions are seen following administration of the drug, one must feel tremendously impressed by any case showing an eruption attributed to the giving of bismuth. I should like more corroborative evidence to establish that this patient is suffering from an eruption due to bismuth before I accept that theory as a diagnosis.

DR. ISIDORE ROSEN: I saw this patient at the time of admission to the clinic when he presented an established case of lupus erythematosus of the face with extensive scarring and atrophy and here and there active lesions. I saw him for a second time after he had received a second intramuscular injection of bismuth. At that time there was decided erythema of the face, neck and upper arms, similar to a severe sunburn. At the end of a week the eruption had become generalized. After three or four weeks it rapidly improved. I wish to stress the fact that the active lesions of lupus erythematosus that were present when the patient was first seen are entirely healed.

DR. SAMUEL PECK: In view of the reality of bismuth eruptions, I think it worth while to report the following case seen in the service of Dr. Rosen at the Mount Sinai Hospital, that of a woman with syphilis who was treated with neoarsphenamine and bismuth. After a number of injections an exfoliating dermatitis developed which was assumed to be due to arsphenamine. Patch tests with arsphenamine were negative. After the patient recovered the Wassermann reaction of the blood was still 4 plus. It was therefore decided to give her bismuth therapy alone. After the first injection of bismuth she had a recurrence of the skin eruption

which was limited to the face, especially around the eyes. The skin of the eyelids and the surrounding area became extremely edematous and erythematous, and vesicles developed which were soon followed by scaling. I forgot to state that while she had the general dermatitis, a bluish-black discoloration of the dorsa of both hands was noticed which persisted up to the time of presentation here. The changes around the eyes lasted a long time. We were unable to persuade the patient, after her second recovery, to submit to further injections of bismuth in order really to prove a hypersensitivity to bismuth.

DR. MARION SULZBERGER: The case reported by Dr. Peck reminds me of two similar cases in which, following mixed treatment with bismuth and neoarsphenamine, an exfoliative dermatitis appeared. After the dermatitis was cured and following renewed injection of bismuth, there was a generalized recurrence. We decided one could not tell whether these were actually eruptions due to bismuth or whether, through the action of bismuth, some new dissemination of the perhaps previously quiescent arsphenamine had been stimulated.

I should like to know the exact name of the preparation used. Was it bismuth subsalicylate; if so, one might consider this a case of eruption due to subsalicylates or salicylates or due to some other ingredient injected with the bismuth (oil, etc.). I believe that only tests can decide this question.

DR. M. B. PAROUNAGIAN: I have no diagnosis to offer in this case, but among many many thousands of injections of bismuth that my associates and I have given, I have never seen an eruption caused by bismuth.

DR. LUDWIG OULMANN: I want to affirm the statements of Drs. Peck and Sulzberger. I had a case which was shown here by Dr. Hopkins, in which an exfoliating dermatitis developed after combined treatment with arsphenamine and bismuth. Any metallic preparation, bismuth or mercury caused a new outbreak of dermatitis.

DR. HERMAN GOODMAN: Does any one know what the patient was loading on the ship where he worked naked and perspiring? Could the dermatitis have been caused by the presence of any toxic agent in the hold of the ship, or among the materials that he handled?

DR. HERMAN FEIT: There was a case of a woman who twice had dermatitis caused by arsphenamine. The arsphenamine was given against my special order and she nearly died from the resulting condition. A year later she reported a positive Wassermann reaction and I decided to give her bismarsen. By the time it was given to her she said: "I think that is the same thing I had before." For the third time a dermatitis developed. I think that Dr. Myers brought out that some bismuth preparations contain a large amount of arsenic. It would be interesting to test this bismuth preparation. Why should the patient be sensitive to arsphenamine and also to bismuth?

DR. G. S. WILLIAMSON, Cleveland, Ohio (by invitation): I am very much interested in this case because I think that eruptions produced by bismuth are extremely rare. Last winter at the Lakeside and the City Hospitals, complications following the treatment of syphilis were investigated. In a total of 410 cases in which there were complications, only a single case was attributable to bismuth. My associates and I were doubtful in that case, and later a diagnostic test was made on two occasions: Both times a mild dermatitis developed, so that we felt quite certain that the condition was caused by bismuth. In the case presented here, after the eruption clears, a diagnostic test should be made by the further use of injections of bismuth.

DR. LAPOWSKI: What kind of bismuth preparations does Dr. Parounagian use?

DR. PAROUNAGIAN: Practically all known forms of bismuth are used.

DR. E. WILLIAM ABRAMOWITZ: Bismuth has been known as somewhat toxic ever since it was introduced as a medicine. In fact, Balzer in 1889 abandoned his experiments to determine the value of bismuth salts in syphilis, on account of the severe reactions produced in dogs, following the use of bismuth citrate.

About ten years ago, the French introduced sodium and potassium tartrobismuthate as an antisyphilitic remedy. A host of other types of bismuth preparations followed when this metal was proved to be of antispirochetal value.

Reports of reactions from bismuth soon appeared, particularly in the French and German literature, and I called attention to these reactions in this country in the May, 1924, issue of the *Medical Times*. In a recent five year survey made by Paul Vigne of Marseilles, he found that of 2,396 patients treated exclusively with bismuth, 202, or 8.8 per cent, were obliged to abandon this form of antisyphilitic therapy, owing to various ill effects. Stomatitis was at the top of the list with an incidence of 72 per cent. Cutaneous eruptions occurred in 5 per cent of the patients who showed reactions and were usually of the type seen in the patient presented here, i. e., erythroderma. The attribution of an eruption to bismuth is usually disputed, as there has been a previous or concomitant use of other antisyphilitic drugs, such as arsenic or mercury. Erythroderma caused by bismuth (meaning a generalized exfoliating dermatitis, as seen following the arsenicals) must be uncommon in the United States, as I have never seen or read a report of such a case. I am at a loss to explain why this is so, as other types of eruption due to bismuth have been reported in this country.

The sequence of events that developed in the patient presented points toward a generalized exfoliating dermatitis due to bismuth salicylate (chemically called bismuth subsalicylate). He had typical fixed patches of lupus erythematosus on his face for many years, which he treated with mild topical applications. A slight itchy eruption developed on his body, which was previously uninvolved, after the first injection of bismuth salicylate; this eruption rapidly became generalized after he received the second treatment. It remains to be seen what influence, if any, the bismuth ointment that he applied to his face had on the outbreak of the eruption, as well as whether there is any significance in the fact that during this period he had been unduly exposed to the sun.

One can exclude the possibility of generalized lupus erythematosus, as in that condition the lesions are of an erythema multiforme type and the constitutional symptoms are quite severe. The patient presented here was only slightly indisposed even though there was extensive involvement of the skin over the entire body. Furthermore, the original lesions on his face for which he was treated are now barely perceptible. The atrophic areas are, of course, still to be noted.

The preparation used for the injections were bismuth subsalicylate, 10 per cent, suspended in wool fat and peanut oil. This is a standard preparation used at the clinic. If the patient permits it, he will be tested to prove his susceptibility to bismuth.

A Case for Diagnosis (Dermatophytosis?). Presented by Dr. Herman Sharlit.

C. S., a white man, aged 42, for two and a half weeks had an eruption, generalized, and also located on the scalp. The diagnoses considered were seborrheic dermatitis and dermatophytosis with trichophytids. Microscopic examination for tinea gave negative results. The trichophyton test was mildly positive. The patient showed a fairly general eruption all over the body, characterized by a slightly elevated, scaly, confluent eruption, eczematized in many portions of the skin. The skin of the feet was macerated, particularly between the toes. At the last moment examinations for tinea were made from scrapings from between the toes, but microscopic examinations for fungi gave negative results. More such examinations will be made. A trichophyton test with polyvalent extract made at the medical school laboratory was slightly positive.

Dr. Samuel Peck: The diagnosis of epidermophytosis with epidermophytids in such a case would rest on a number of factors: 1. In order to make a positive diagnosis, instead of a presumptive one, of fungus infection the fungi, of course, must be demonstrated. The fungi should be found in the primary lesion and not in the trichophytids in the average case. The most difficult thing in a case of this kind is to make up one's mind where to look for the fungi, as it is almost

impossible to determine where the epidermophytosis ends and the epidermophytids begin. Even in the primary lesions it is often possible to find the fungi only by culture. 2. The trichophyton reaction should be strongly positive. While it is conceivable that there may be a positive anergy it is not the rule. 3. A flaming up of the trichophytids, even in the presence of a moderately positive trichophytin, is one of the best proofs for a diagnosis of epidermophytids. If one takes the casual dermatologic cases as they come in to the clinic in more than 50 per cent a moderate degree of hypersensitivity to trichophytin is found; therefore, on a moderate reaction alone a diagnosis cannot be made. The control for the trichophytin must be used in the correct dilution to obviate pseudoreactions, and if the diluted trichophytin is allowed to stand too long it loses its potency. About a year and a half ago I described a case with hemorrhagic trichophytids on the legs which developed after injections of trichophytin.

DR. MARION SULZBERGER: There is one additional point that seems to me to be of increasing importance for the conception of these eruptions, which has been brought out by Ravaut and in the work of Hopkins and others. Eczematous reactions to monilia and oidiomycetes as well as to other types of fungi can occur. I am sure that a fair percentage of dyshidrotic eczemas and "ids" are due not only to Trichophyton and Epidermophyton, but to Monilia and other fungi. There are probably also many cases of mixed infections. These different fungi seem to be able to cause clinical pictures that are often indistinguishable. I have tested many patients with both oidiomycin and trichophytin; some react to only one fungous product and some to both. Naturally specific desensitization must be directed against the fungus or fungi responsible in each case.

DR. HERMAN FEIT: Dr. Ravault of Paris pointed out that different fungi may produce the same clinical picture and that the same fungus may produce different clinical pictures. One might make a diagnosis of trichophytid and the condition might be caused by Monilia. He warned against being too optimistic in regard to therapy with the levurines.

DR. HERMAN GOODMAN: I think that we are going far afield in this case. The reaction to trichophytin in this patient has been reported doubtful. Why the discussion on trichophytin? No laboratory confirmation has been offered for the clinical diagnosis of a primary focus of trichophytin elaboration. Without that, the diagnosis of trichophytid has no place. In the absence of any proved etiologic factor and in the presence of a cutaneous response to insult which is common to dermatitis and eczema, it should be reasonable, even though perhaps old fashioned, to regard the condition as eczematization. The treatment should be directed to relieve the symptoms, empiric as that treatment may be. This will result in amelioration sooner than treatment with remedies designed to destroy parasitic invaders that are not found.

Doubtful, mildly positive or even strongly positive reactions to trichophytin should not be taken as absolute evidence of the presence of mycotic invasion, and certainly not as proving the parasitic or paraparasitic nature of every cutaneous eruption. Positive reactions to trichophytin have been found in clinical cases of pityriasis rosea. Some of the patients did and others did not have cryptic ringworm infections between the toes. The trichophytin should also be cultured periodically, as contaminated trichophytin gives bizarre results.

DR. ISIDORE ROSEN: I agree with the diagnosis of dermatophytosis with generalized dermatophytid.

Since the knowledge of dermatophytosis and of its toxic secondary manifestations has increased during the past few years, one is more familiar with the polymorphism of these infections. Whereas heretofore in many cases the diagnosis was eczema, seborrheic dermatitis, neurodermatitis, psoriasis or a similar condition, such conditions are now known to be one of the complications of dermatophytosis.

During the past few months, I have been able to follow in my private practice a few cases of typical dermatophytosis of the feet with generalized papulovesicular, erythematous, squamous and eczematized lesions, including lesions of the face

and scalp, in which constitutional symptoms were present, such as low grade fever, headache and malaise which lasted for a week or more.

A Case for Diagnosis (Telangiectasis?). Presented by Dr. Herman Goodman.

A. J., a woman, aged 54, was admitted to the clinic of the Stuyvesant Square Hospital on Sept. 19, 1931, at which time she complained of a red, thickened eruption occurring on her neck each summer and lasting from three to four months. This was of four years' duration. On examination, telangiectatic areas were noted over the angles of the mandible. Of these the patient was unaware. The family history and past history were essentially unimportant. The menopause had occurred ten years before admission.

The blood count showed hemoglobin, 65 per cent, and red blood cells, 4,400,000, and the Wassermann reaction was negative.

Biopsies: A section from the telangiectatic area showed a thin epidermis with no rete pegs. There was a very thin corneum. Some of the granular cells were swollen and enlarged. Scattered throughout the corium were numerous sebaceous glands and a few dilated blood vessels. These vessels were surrounded by a very slight exudate. The collagen fibers seemed to take a basophilic stain and many were swollen. Section from normal tissue showed a thin epidermis with rete pegs. There was a vesicle in the epidermis. The blood vessels were not especially dilated but were surrounded by round cell infiltration. Many of the collagen fibers took a basophilic tinge.

DISCUSSION

Dr. Max Scheer: The only lesions that I could see were a few telangiectasia in the region of the angle of the jaw. The poikiloderma of Civatte can be excluded because there is no reticulation, pigmentation, etc.

Dr. A. Benson Cannon: I think the condition is a type of skin seen after continued exposure, such as "sailor's skin," or possibly is caused by the constant reflexion of a lamp bulb.

Dr. Charles Lerner: I am inclined to agree with Dr. Cannon's remarks. On careful questioning the patient told me that she has been continuously exposed to the weather a good deal during the past five or six years. If I am correct in my recollection, the duration of her condition is approximately that length of time. Furthermore, the eruption on the other side of the neck appears somewhat similar to me, although not quite so pronounced. Were the patient a man, I think one would not hesitate to call the condition an incipient "leather neck" or "sailor's skin."

Dr. Herman Feit: I had the same impression as Dr. Scheer. Going into the history in this case I find that the eruption is of an evanescent character, which excludes the diagnosis of poikiloderma.

Dr. Herman Goodman: The patient reported to the hospital a little over a month ago. At that time, as now, the most confusing aspect of the cutaneous condition was the appearance at the angles of the jaws and the skin contiguous to them. There was, and is, distinct mottling and telangiectasia. Below the angles of the jaws and running back to the midline of the neck, she had a definite vesiculation, the result of an immediate response to insult or dermatitis. Clinically and under the microscope the skin from the neck in no way resembles that from the angle of the jaw. The appearance of the discoloration and dilated capillary vessels is reminiscent of a similar case shown before this section some years ago: Dr. Highman suggested the possibility of Majocchi's disease at that time. I cannot agree with such a diagnosis in this case, and asked the patient to report this evening.

Lupus Erythematosus or Sarcoid (?). Presented by Dr. Joseph Morse.

This case was presented before the Section on Dermatology and Syphilis at the November, 1931, meeting.

DISCUSSION

DR. MARION SULZBERGER: Dr. Morse and Dr. Gross asked me to report on this case. The differential diagnosis rested between sarcoid and some other form of tuberculoma. Further investigation showed that the histology of the lesions on the hand was typical of sarcoid. Roentgen examination of the hands, which Dr. Gross suggested should be made at that time, showed the typical picture of osteitis cystica of Jüngling. The picture of the lungs also was typical of the roentgenogram of the lungs usually found in sarcoid.

At autopsy these changes in the lungs were found to be typical epithelioid tubercle changes. The Wassermann reaction was negative. Chemical examination of the blood also gave negative results. The tuberculin test was negative with a dilution as great as 1:1,000, which is another finding that is typical of this type of sarcoid. All in all, this case seems to have been a textbook example of sarcoid.

POIKILODERMIA ATROPHICANS VASCULARIS. Presented by DR. EUGENE TRAUB.

J. R., a man, aged 39, married, born in the United States, an employee of a railroad, had an unimportant family history. He had used Ex-Lax four times a year and had been using bromo-quinine infrequently since 1916. His condition had been present for from a year and a half to two years.

On admission, May 20, 1931, the patient presented six patches on the abdomen, about 5 inches (12.7 cm.) long and 4 inches (10.16 cm.) wide, sharply demarcated, with surrounding inflammatory zones and atrophic centers and with advancing margins which were distinctly elevated. There was telangiectasis in the region of the atrophic changes. About the border of the patches, the skin was dry, scaly and hyperkeratotic. There were also erythematous patches on the inner side of the arms and axilla, which were probably early lesions as they showed some tendency to atrophy.

The laboratory reports showed a negative Wassermann reaction. Chemical examination of the blood showed 9.6 mg. of urea nitrogen, 3.33 mg. of uric acid, 86.8 of sugar and 471 mg. of chlorides per hundred cubic centimeters.

Biopsy showed a thin epidermis with no rete pegs. There were horny plugs in the follicle openings. The basal cell layer was irregular. The blood vessels were dilated, and there was much edema between the connective tissue fibers in the upper corium. Round cell infiltration that was not perivascular was present in the upper corium. The round cell exudate was lymphatic.

The patient received wool fat ointment and tar and zinc ointment and improved under that therapy.

DISCUSSION

DR. HOWARD FOX: I think that this case could be classed as one of poikiloderma vasculare atrophicans or at least in a group closely related to this rare infection. Some of the patches suggest the appearance of parapsoriasis, though I do not consider the condition to be this disease. There are definite areas of telangiectasis and atrophy. The condition does not present the picture of radiodermatitis as there is no pigmentation. The appearance of this patient suggests an endocrine disturbance, and doubtless the eruption is due to this cause. The possible relationship to endocrine dysfunction has been pointed out by Bloch in a somewhat similar case.

DR. FRED WISE: I agree with Dr. Fox. The simulation of the abdominal lesion to a radiodermatitis, is a characteristic feature of the eruption as seen in poikiloderma of Jacobi. A case of this type must be kept under observation for a long period of time in order to arrive at a definite clinical diagnosis of the cutaneous condition.

DR. EUGENE TRAUB: Naturally this case will have to be followed in order positively to substantiate this diagnosis. When my associates and I first observed the patient, a diagnosis of localized scleroderma or morphea was considered, but microscopic examination seemed definitely to rule out this condition. Parapsoriasis was not considered because of the atrophy and the lack of any definite scaling. The patient has had no subjective symptoms, and was not aware of the presence

of the eruption until his attention was drawn to it. Of course, the absence of itching does not necessarily rule out a premycotic eruption, but certainly speaks against this diagnosis. The amount of atrophy present so early in the course of the disease would seem to my mind also to be against the possibility that the condition is early mycosis fungoides. Cases, however, have been reported that in their inception presented the picture of poikiloderma, but subsequently became characteristic of mycosis fungoides.

HYDRO VACCINIFORME (?). Presented by DR. DAVID BLOOM.

S. A., a boy, aged 5 years, was seen for the first time in April, 1931, with an eruption which had started at the age of 6 months, and had recurred since then every summer. The warmer the weather the worse the eruption became. It consisted of papules and vesicles on an erythematous and edematous base. Many lesions were covered with hemorrhagic crusts; others showed, under the fallen crust, a central depression. The eruption was located mainly on the face (ears, temples, forehead and cheeks) and on the extensor surface of the hands, forearms and arms. It was present to a lesser degree on the legs, chest, shoulders and remainder of the trunk. A few depressed ulcers were seen on the mucous membrane of the cheeks. Besides, there were numerous pitted scars, mainly on the face, and one large scar, 1 by 1½ inches (2.5 by 3.7 cm.), between the eyebrows.

The itching seemed to be moderate, but the patient felt uneasy. The temperature varied from normal to 101 and 103 F. The urine showed at one time numerous white blood cells and a marked trace of albumin. The blood count showed 7,000 white blood cells and 4,000,000 red blood cells. Hematoporphyrin was not found in the urine.

The family and personal histories were unimportant.

DISCUSSION

DR. HOWARD FOX: Over the extensor surface of the arms there are small pitted scars reminding one of a papulonecrotic tuberculid. Has this condition been excluded in any way?

DR. MARION SULZBERGER: I think that in some atypical cases of hydroa vacciniforme or prurigo aestevale the diagnosis of atypical papulonecrotic tuberculid should be considered. This is particularly true in cases such as this one, in which the covered parts of the body are also affected. Papulonecrotic tuberculids often appear in the spring and summer months and disappear in the winter months. It has been learned now that a typical tubercle is not always found in excising a lesion of this type of tuberculid. The stage in which the excision is made determines whether one will find tubercle structure or not.

There are some factors throwing weight in favor of a diagnosis of papulonecrotic tuberculid. One is, of course, the lung; if it is absolutely normal, that is, shows no signs of even a mild healed infection, one can always exclude papulonecrotic tuberculid, unless one has definite evidence of tuberculous infection elsewhere.

The quantitative tuberculin reaction, dilutions of from 1:1,000,000 to 1:500 or more being used, is another great aid. It is usually either strongly hypersensitive or hyposensitive. Both of these typical reactions speak in favor of a diagnosis of papulonecrotic tuberculid. The child presented this evening also has a large gland on the back of the neck.

DR. DAVID BLOOM: The clinical appearance of the eruption in April and the course of the disease since the age of 6 months are typical of hydroa vacciniforme. The involvement of the trunk does not speak against that diagnosis. In this case, the exciting cause seems to be the heat more than the actinic rays, as there is a history of marked development of the eruption on warm days, even if the patient remains at home. This may also explain the slight involvement of the trunk. The fact that no hematoporphyrin was found in the urine does not speak against the diagnosis of hydroa vacciniforme.

It has been found by Perutz that the elimination of hematoporphyrin is intermittent, and repeated examination of the urine may prove the presence of hematoporphyrin. Also there is the possibility of the presence of porphyrinogen instead of porphyrin, which does not show spectroscopically. I do not know of any case of hydroa vacciniforme in the literature found to be tuberculous.

For the sake of completeness, however, the boy will be examined for tuberculosis and, also, if possible his skin will be tested for sensitiveness to actinic rays.

KERATOSIS PALMARIS ET PLANTARIS HEREDITARIA (OCCURRING IN FOUR GENERATIONS). Presented by DR. DAVID BLOOM.

T. N., a girl, aged 4 years, showed on her soles a few circumscribed yellow, translucent, thick, horny plaques, from the size of a dime to that of a half-dollar, located on the heels, plantar surface of the large toe and tip of the little toe. The toe-nails were thickened. On the left palm there were a few keratoses the size of a pinhead. The keratoses on the soles developed at the age of about 1½ years when the child had started to walk. Her father, who was presented together with the girl, her grandfather, her great-grandfather and other members of their families were similarly affected.

There was no hyperhidrosis of the palms or soles. I had seen personally the patient's father and an uncle (the brother of her father) who showed a similar condition on his feet but only a few keratoses on his hand.

KERATOSIS PALMARIS ET PLANTARIS HEREDITARIA (OCCURRING IN FOUR GENERATIONS). Presented by DR. DAVID BLOOM.

C. N., a man, aged 46, a Greek, showed thick yellow, translucent keratotic plaques from the size of a quarter to that of a small palm on the balls of the soles and on the heels. These lesions had started when the patient was about 1½ years of age when he started to walk. The toe-nails showed marked thickening. The palmar surface of the fingers showed numerous keratoses, some the size of a pea and others the size of a hazelnut, as did the palms themselves. The involvement of the hands became marked when the patient started to exercise his occupation as a shoemaker. There was no hyperhidrosis of the palms or soles. The patient had one daughter, aged 4 years, who had become similarly affected and who was presented together with him. A son, 6 months old, did not show any abnormality. The patient's father and grandfather had had the same condition, and also other members of their families. There was no history of consanguinity.

BOWEN'S DISEASE (?). Presented by DR. PAUL GROSS for DR. KESTEN.

M. R., a woman, aged 75, a German, had been admitted to the Vanderbilt Clinic on Nov. 18, 1931, with a history of a reddened nodule on the left side of her face, of nine and a half months' duration. At that time the lesion was about the size of a pea and was not elevated. For about four and a half months after its appearance the nodule had not changed in size but then a yellowish-white crust appeared, which had been removed by the patient's own physician. During the five months prior to presentation the lesion had increased in size very slowly. There had never been any pain or swelling.

Over the left zygomatic process there was a circular and sharply demarcated nodule about 1.5 cm. in diameter. This nodule was composed primarily of a thick crust which when removed left an oozing base which was not so well demarcated. The lesion was not fixed to the underlying tissue, nor was there glandular involvement of the regional nodes. On the surface of the nose there was a diffuse reddened scaly eruption spreading to the labial folds. The patient had received roentgen therapy consisting of four unfiltered doses.

Biopsy: A section was suggestive of Bowen's precancerous dermatosis, but, in view of the intense inflammatory reaction, it was a little difficult to be sure

that this was the primary condition, and that the dyskeratosis was not secondary to the inflammation noted in the corium.

TINEA CIRCINATA HERPETICA (HERPES CIRCINATUS). Presented by DR. CHARLES LERNER.

M. N., a girl, aged 10, born in the United States, first called at the New York Post-Graduate Hospital skin clinic on Nov. 30, 1931. Her condition had existed for one week.

On examination, the patient presented over the front of the chest, arms, forearms, back and face numerous circular lesions from the size of a pea to that of a dime with clearing centers and erythematous scaly and vesicular peripheries. Within the centers of some of the lesions, however, there were erythematous spots the size of a pinhead.

There were three brothers who showed a similar condition in the early stages. Examination for tinea gave positive results.

BOWEN'S PRECANCEROUS DERMATITIS. Presented by DR. PAUL GROSS for DR. KESTEN.

F. R., a woman, aged 41, a Russian, had been admitted to the Vanderbilt Clinic on Nov. 23, 1931. She gave a history of a growth which had begun on the trunk five years previously. At first a pimple formed, and then a scaly patch which itched somewhat. When the patient removed the scales because of itching, the lesion bled a little. About four years prior to presentation, it had been somewhat smaller than at the present time but much more raised and scaly. The patient sought relief at a local clinic. There a diagnosis of psoriasis was made and two ointments were prescribed. Following the application of these for a year and a half there had been definite improvement, but the lesion did not clear. The patient then applied a third ointment for some time. This relieved the itching, and some of the scales had disappeared from the center, but the patient believed that the patch was spreading. No similar lesions had appeared on other areas. In addition to the pruritus the patient stated that this area was tender on pressure. Her general health was good. There had been no history of internal medication.

On the right side of the trunk at about the middle third, in the midaxillary line, there was one irregularly rounded plaque measuring 5.5 by 4 cm. It was an isolated erythematous area mostly covered with small irregular white and yellowish crusts and with a distinctly raised lower and lateral border. The initial lesion appeared to be a papule. There were two isolated ones at the lateral border of the patch, which were purplish red, flat topped and moderately firm. The lower border of the lesion was a continuous slightly irregular line 3 cm. in length and 0.75 cm. wide. It was the same color and consistency as the papules and appeared to have been formed by the coalescence of similar papules. The center of the lesion was less erythematous and infiltrated than the surrounding area, and there were accentuation of the lines of cleavage and superficial scaling. The crusts covering the rest of the lesion were slightly adherent and when they were removed the areas left were found to be covered with punctate hemorrhages which did not ooze. The entire lesion was moderately firm and tender on pressure.

The rest of the skin was clear except for a number of nevi (vascular and fibrous). The scalp was clear, and there was no stippling of the nails.

A specimen was removed from the lower border of the lesion for biopsy. Sections showed superficial vesicle formation with marked parakeratosis. An acanthosis was found to be present. The epithelium contained large numbers of swollen dyskeratotic cells many of them having the appearance of corps ronds. Groups of these cells suggested a pearl formation. Numerous atypical mitotic figures were seen. Several multinuclear epithelial cells were seen which suggested clumping cells. There was moderate infiltration of the corium with lymphocytes and plasma cells. There was marked edema of both epithelium and superficial corium.

PEMPHIGUS. Presented by DR. HERMAN GOODMAN.

S. K., a woman, aged 56, was seen for the first time in the Stuyvesant Square Hospital clinic on Nov. 10, 1931. She complained of a burning sensation in the mouth of six weeks' duration, which, at its onset, had appeared only at night, but later had become constant. The pain was so severe as to prevent sleep; it was aggravated by eating solid food. At the time of onset, blisters were noticed on the gums, and there was a heavy yellowish coating on the tongue.

Four weeks before the patient's admission to the clinic, the blisters healed, under treatment by her physician, but in a short time they reappeared and the pain was increasingly severe. Salivation became much increased. The patient had lost 4 pounds (1.8 Kg.) since the onset of her illness. The family and past histories were essentially unimportant.

At the time of her first visit to the clinic, the patient showed numerous erosions and the remains of the edges of bullae on the mucosa of the cheeks, lips, palate and floor of the mouth. These lesions bled easily. The tongue was heavily furred, and there were many long and short hairs. There was no involvement of any other part of the body.

On Nov. 24, 1931, the mouth showed improvement and the tongue was almost clean. For the first time, however, several broken vesicles and one unbroken one were found on the upper part of the midback and the right arm.

Laboratory Examinations: The blood count showed: hemoglobin, 60 per cent; red blood cells, 4,000,000, and white blood cells, 11,200, with polymorphonuclears, 72 per cent, lymphocytes, 27 per cent and basophils, 1 per cent. Examination of the urine showed nothing abnormal. Chemical examination of the blood showed: urea nitrogen 10.8 mg., uric acid, 2.38 mg., sugar, 92 mg. and chlorides, 437.7 mg. per hundred cubic centimeters. The Wassermann reaction of the blood was negative.

Microscopic examination of scrapings from the tongue on Nov. 10, 1931, showed only hairs and débris. A culture was made and examined two weeks later which showed only staphylococci.

ERYTHEMA ANNULARE CENTRIFUGUM. Presented by DR. HERMAN GOODMAN.

E. O., a woman, aged 33, married, a Russian, had been seen for the first time on Oct. 6, 1931, at which time she presented annular patches with raised erythematous scaling borders on the abdomen and chest. The lesions were associated with burning pain while they were developing; the pain disappeared as the condition improved. Similar lesions had recurred, at varying intervals, for twenty-one years; the duration of the lesions seen on the patient's admission to the clinic was one year. Chemical examination of the blood gave essentially normal results. The Wassermann reaction was negative. Biopsy was done, but no diagnosis was made: The section showed an irregular epidermis; there were edema in the upper corium, dilatation of the blood vessels and a basophilic tinge of the whole section.

The condition improved, under treatment with boric acid ointment. On Nov. 17, 1931, the patient showed new but similar lesions on the right side of the chest; the old lesions were still present at this time. No diagnosis was made. A section showed an almost normal epidermis and, within some areas, moderate intercellular edema of the prickle cells and some tendency to ballooning degeneration. The upper third of the corium took a pale stain, and there was marked intercellular edema and slight round cell infiltration about the blood vessels, which were engorged. The vessels in the lower corium were also engorged and surrounded by a somewhat more dense round cell infiltration, and the collagen fibers took an intense acid stain; a section taken for biopsy showed an exudative process.

MYCOSIS FUNGOIDES. Presented by DR. EUGENE TRAUB.

This case was presented before the Section on Dermatology and Syphilis at the November, 1931, meeting.

DISCUSSION

DR. EUGENE TRAUB: The members may recall that when this patient was presented at the last meeting, she had been seen in the dispensary on that same day for the first time. Therefore, there were no data, and the tentative diagnosis was based solely on the clinical appearance of the eruption. Even the history was not very reliable, and it was not until later that we learned that the patient had received thirty exposures to ultraviolet rays and no roentgen therapy for the lesion on the abdomen, the question having arisen as to what form of radiation the patient had received. Since her presentation, a number of biopsies have been performed, and these were submitted to the pathologists of the New York Skin and Cancer Hospital, to those of Mount Sinai Hospital, and to Dr. Walter James Highman. In each instance the diagnosis of mycosis fungoides was returned.

The clinical course in the past month has also helped definitely to establish the diagnosis of mycosis fungoides. A small fungating tumor appeared on the left shoulder, reached the size of a small walnut and then receded under treatment with boric acid ointment locally and arsenic internally. A number of small nodules have developed such as are commonly seen in this disease over the trunk and extremities. Although her only treatment has been tonic—rest in bed with bland ointment locally—she has greatly improved since her last appearance at this Section.

SCARS. Presented by DR. HERMAN GOODMAN.

F. R., a girl, aged 15, following variola at the age of 3 months, had had scars on the face, arms and back. No new scars had appeared, as far as she could recall; the old ones had become smaller in recent years. The family history was unimportant except that the grandmother had diabetes. The patient had had her left eye removed one year prior to presentation; this eye had been blind since an attack of smallpox. The further history was unimportant.

DISCUSSION

DR. HERMAN GOODMAN: The patient had smallpox at the age of 3 months. The scars have persisted since that time. Despite persistant questioning, no history of recurrent attacks of scar-forming skin eruptions could be secured. I had thought of the possibility of summer eruptions with scarring. The patient is anxious for relief from the rather repulsive appearance. I doubt whether any means at my command will be effective in procuring improvement in the patient's condition.

MINNESOTA DERMATOLOGICAL SOCIETY

Dec. 2, 1931

H. N. KLEIN, M.D., *President, Presiding*

A CASE FOR DIAGNOSIS (LUPUS ERYTHEMATOSUS). Presented by DR. H. E. MICHELSON.

M. O'G., a white woman, aged 67, had carcinoma of the breast which had been untreated until after the eruption developed, but which had since been treated with radium. Following exposure to the sun's rays in September, 1931, an eruption developed on the forehead, nose and nasolabial folds, circumoral region (with a sharply marginated area of pallor within), neck and exposed portion of the chest, and discrete lesions appeared on the dorsa of several fingers and of the thumbs. The eruption had changed somewhat from day to day, but there was no marked progress or regression. This condition was presented as erythema with some dilatation of follicular openings; on the neck there were pinhead-sized follicular

papules. A roentgenogram of the chest showed minimal fibroid tuberculosis of the upper lobe of the right lung and probable pleural effusion in the base of the left lung. Biopsy showed hyperkeratosis with some plugs in dilated follicular orifices and dilated vessels in the corium with a surrounding lymphocytic infiltrate.

DISCUSSION

DR. HAMILTON MONTGOMERY (Rochester): The histopathologic picture shows all the features of acute disseminate lupus erythematosus.

DR. H. F. MICHELSON: This is the second patient we have seen who had a typical case of lupus erythematosus and an internal malignant condition. I do not know what the relationship is, but it seems to be more than casual.

DR. J. F. MADDEN (St. Paul): Four of ten patients whom we have recently studied stated definitely that the eruption appeared immediately following marked sunburn or chronic lupus erythematosus which became acute following sunburn or actinic therapy. Photosensitivity plays a major rôle in some of these cases.

DR. W. H. GOECKERMAN (Rochester): I saw a case of disseminate lupus erythematosus last summer in which the photosensitiveness was so pronounced that following exposure to ordinary summer sunlight the patient showed an eruption over the areas covered by his shirt but not over the areas covered in addition by his underwear. The rays penetrating his shirt were sufficient to bring out a typical eruption. A minor degree of photosensitiveness is not uncommonly seen.

DERMATOFIBROSARCOMA PROTUBERANS (DARIER, HOFFMAN). Presented by DR. H. E. MICHELSON.

A. W., a white woman, aged 50, first noticed a firm nodule on the anterior abdominal wall in 1909, which was surgically removed one year later, when it had become the size of a hen's egg. The growth recurred, and was again removed in 1912; it recurred later, but there was always only one tumor until about 1926. At that time there were a number of lesions and some of them became sessile and ulcerated. They were removed, and recurred soon afterward. Excision and roentgen therapy were carried out in 1928 and May, 1931. An examination made in November, 1931, showed several orange-sized, ulcerated, cauliflower-like masses and several hundred firm nodules and tumors of the skin on the anterior abdominal wall extending to the thighs and perineum. There was severe anemia, with 36 per cent hemoglobin.

The first biopsy reported in 1928 showed sarcoma of an undetermined type. The second biopsy, performed in 1928, showed myxosarcoma. In May, 1931, the biopsy report was spindle cell sarcoma; and in November, biopsy showed spindle cell sarcoma and some myxomatous degeneration.

DISCUSSION

DR. H. E. MICHELSON: This condition is evidently an entity. It was first described by Darier and Hoffman; in this country it was first described by Senear. The condition begins with nodules which involve both the skin and the subcutaneous tissue. The course is extremely long, lasting for years. Gradually the process seems to take on a more markedly malignant character. This is the second patient with this condition whom I have seen in our service. The other patient had had the lesions for more than twenty years, but finally succumbed to the condition. In the case presented the prognosis is poor.

A CASE FOR DIAGNOSIS (LYMPHOBLASTOMA?). Presented by DR. H. E. MICHELSON.

Dr. H. T. E., a white man, aged 69, first noticed an eruption on the thighs and scrotum in January, 1930. The eruption had spread and involved all extremities, but it was most marked on the flexor surfaces. The lesions consisted of

papules, occasional vesicles, fissures and excoriations on a brightly inflammatory base. There was temporary involution under roentgen therapy. Examination of the blood showed 11,700 white cells, with 55 per cent lymphocytes, which were slightly toxic but showed no evidence of immaturity.

DISCUSSION

DR. W. H. GOECKERMAN: I believe that this is a case of lymphoblastoma. Subclassification in such cases is often exceedingly difficult. Not uncommonly the syndrome of a given type changes into that of another as time goes on.

DERMATITIS EXFOLIATIVA FOLLOWING PSORIASIS. Presented by DR. S. E. SWEITZER.

H. G., a white woman, aged 43, presented a condition of the skin which had first appeared three years previously as reddened patches on the knees, elbows and scalp, covered by lamellar scales. The course had been one of remissions and frequent recurrences. Two months before presentation she had a recurrence and began to receive treatment. The condition became acute and progressed to complete exfoliation. There was no arthritis. The Wassermann reaction of the blood was negative. The treatment consisted of daily applications of a mild tar ointment, combined with a daily light treatment, as outlined by Dr. Goeckerman. Under this regimen the patient has shown marked and steady improvement. She has been under treatment now for almost a month. A specimen was taken for biopsy.

DISCUSSION

DR. JOHN BUTLER (Minneapolis): Previously, the condition may have been psoriasis, but now it is an arsenical keratosis. I saw the patient about four weeks ago, and in taking the history I found that she had been taking solution of potassium arsenite in doses of 15 drops for about a year. The palmar and plantar condition is typical of arsenical keratosis.

DR. S. E. SWEITZER: We had two patients with exfoliative dermatitis in the hospital at the same time. This patient did not improve. Dr. Laymon asked whether he could try Dr. Goeckerman's treatment with crude coal tar, and when he did, definite improvement occurred. An acute exfoliative dermatitis was present, which, according to the history, had not appeared until some salve had been used. The patient has improved steadily under the treatment advocated by Dr. Goeckerman. When she came to the hospital we were unable to see the arsenical keratosis on account of the edema of the skin. I presented her merely to show the improvement under this treatment.

DR. H. MONTGOMERY: In this case the histologic picture is typical of psoriasis. Sections revealed no evidence of an arsenical pigmentation or keratosis, which of course, does not exclude the possibility of arsenical keratoses, which were obviously present clinically.

DR. W. H. GOECKERMAN: In a recent review of our series of erythroderma psoriatica, I confirmed the observation that arsenic administered in almost any of its forms, irritating ointments and acute or chronic infections are responsible for this complication of psoriasis. In our series it seemed as though these factors shared the responsibility equally. It emphasizes the importance of the judicious rather than the routine use of chrysarobin and arsenic. Crude coal tar and ultraviolet rays can be used successfully on the ambulatory patient if he cooperates well.

ACANTHOSIS NIGRICANS (JUVENILE TYPE). Presented by DR. H. E. MICHELSON.

Mrs. R. S., a white woman, aged 31, had noticed a gradual increase of pigmentation in the axillary and perineal regions. Thorough physical examination showed no evidence of an intra-abdominal tumor. The past history was irrelevant except for cesarean sections performed in 1924 and 1926, removal of a vaginal tumor in January, 1931, and irregular menses following operation.

Biopsy showed acanthosis, hyperkeratosis, increased pigmentation in the basal cells and lower prickle cells and perivascular lymphocytic infiltration.

A Case for Diagnosis (Pyoderma, Blastomycosis?). Presented by Dr. J. F. Madden.

R. K., a school girl, aged 11, stated that she had a condition diagnosed as impetigo contagiosa in September, 1931. All of the lesions involuted except the four now present on the right thigh. These lesions are vegetating, soft, verrucous-topped papules on nodules, varying in size from that of a dime to that of a silver dollar. They exude pus on pressure; they are sharply demarcated and slightly painful. The Wassermann test of the blood was negative. Examinations for blastomycetes gave negative results. Biopsy showed abscesses in the epidermis, acanthosis, edema and perivascular infiltration with polymorphonuclears and lymphocytes.

DISCUSSION

Dr. S. E. Sweitzer: I thought that the condition was dermatitis vegetans.

Dr. J. F. Madden: The eruption has not responded to local treatment. We have used all the usual remedies, and the eruption has not altered appreciably in a month.

Dr. S. E. Sweitzer: A patient with a similar case was cured by the administration of roentgen rays in small doses.

Lymphosarcoma or Hodgkin's Disease. Presented by Dr. J. F. Madden.

R. R., a white man, aged 26, first noticed a pruritic eruption in 1929. One year later a mass developed in the left axilla, which gradually enlarged until it is now the size of an orange. He gives a positive Wassermann reaction and he has been receiving antisyphilitic therapy as a routine. For the past three months he has noticed loss in weight and general malaise accompanied by a low grade fever.

Examination showed an orange-sized mass of matted glands in the left axilla, probable widening of the mediastinum and a palpable and tender spleen. There was a marked dryness of the skin, with a vesicular and papular eruption on the flanks and the flexor surfaces of the extremities. There were several atrophic polycyclic scars on the lower extremities. The patient had recently been treated for molluscum contagiosum. He had secondary anemia. A blood count showed 12,500 white blood cells, with 59 per cent polymorphonuclears (a normal percentage). Biopsy of the axillary mass performed by Dr. E. T. Bell showed lymphosarcoma.

Note.—Further observation established the diagnosis of Hodgkin's disease.

DISCUSSION

Dr. H. E. Michelson: The microscopic diagnosis is lymphosarcoma, but because of the clinical symptoms, a diagnosis of Hodgkin's disease, lymphosarcoma type, has been made.

Dr. W. H. Goeckerman: As Dr. Michelson said, the section showed an infiltrate penetrating the muscle, and Dr. Bell thought that radium should be applied. In my experience, roentgenotherapy is always worth while in cases of this type.

Dr. H. Montgomery: In our experience at the clinic, lymphosarcoma involving the skin may sometimes have a protracted course, but there is always a fatal termination. Death may result in a few months or sometimes after a period of years.

Dr. J. F. Madden: The axillary mass decreased a great deal in size while the patient was under antisyphilitic therapy. Dr. O'Leary stated that he had seen this occur in other cases of lymphosarcoma.

DR. H. MONTGOMERY: In a small group of cases seen at the clinic, Hodgkin's disease seemed possibly to have an infectious basis. In about 85 per cent of the cases, however, the response to roentgen therapy is similar to that seen in cases of lymphosarcoma, and the histologic picture in the glands seems to be merely a variant of lymphosarcoma.

ICHTHYOSIS HYSTRIX. Presented by DR. H. E. MICHELSON.

When the patient, a white girl, aged 2 years, was 8 months old she suffered a great deal from miliaria during the summer. As this condition cleared up the mother noticed a brownish linear eruption on the anterior surface of the right arm. Following this the same type of eruption appeared at the base of the spine, and later it developed in the left axilla. Treatment at home with zinc oxide was given. Water and heat are irritating to these areas. There are periods of spontaneous remission and exacerbation. The patient was first seen by a physician on Dec. 2, 1931.

DISCUSSION

DR. S. E. SWEITZER: This condition has not occurred in the family as far back as we can discover.

DR. H. E. MICHELSON: I once saw a pair of twins one of whom had marked ichthyosis while the other was normal.

DR. J. F. MADDEN: I did not investigate the family history in detail.

LUPUS ERYTHEMATOSUS, CHRONIC. Presented by DR. S. E. SWEITZER.

In a white woman, aged 42, the condition began in May, 1927, as a small patch the size of a pinhead on the forehead just above the eyebrows. Over a period of two months the lesions spread to their present extent. The Wassermann test was negative. Marked improvement in the condition occurred under bismuth therapy. Weekly intramuscular injections of 2 cc. of a suspension of bismuth salicylate in oil and local application of ointment of bismuth oxychloride were administered. Biopsy gave results typical in this condition.

LUPUS ERYTHEMATOSUS (SCALP). Presented by DR. J. F. MADDEN.

Mrs. F. K., a housewife, aged 26, stated that she first noticed a small patch of baldness on the crown of her head four years prior to presentation. The condition gradually progressed to the size presented. She has received only local treatment. The patient presents a partially bald patch about the size of a grapefruit in the frontal and vertical portion of the scalp. There is some hair remaining in this region, but most of it is broken and short. The patch is studded with atrophic scars. The border of the active portion is erythematous. The follicular orifices are dilated and plugged with a fine, dry scale. Examination of fresh scrapings and cultures gave negative results for fungi. The Wassermann test of the blood was negative. The Mantoux test was negative. There was no evidence of tuberculosis. A biopsy was unsatisfactory.

DISCUSSION OF CASES OF LUPUS ERYTHEMATOSIS

DR. S. E. SWEITZER: My patient was shown chiefly to demonstrate the benefit obtained by the use of bismuth. She shows tremendous improvement.

DR. H. E. MICHELSON: In my experience the treatment of lupus erythematosus of the scalp has not been satisfactory. Such lesions do not respond as well as do lesions on the glabrous skin.

DR. J. BUTLER: How do you exclude the pseudopelade of Brocq?

DR. J. F. MADDEN: The erythematous raised border associated with dilated plugged follicles was thought to be enough to exclude pseudopelade of Brocq. Sodium hydroxide preparations and cultures of the hairs and scales failed to reveal fungi.

DR. L. H. WINER: Clinically, I did not see lupus erythematosus of the scalp, which would show a more red cyanotic border. The scalp in this area appeared to me to be rather tense, and the failure to find crusts, which is a characteristic of favus, would make me lean toward Dr. Butler's diagnosis of pseudopelade of Brocq.

DR. J. F. MADDEN: Local medication containing sulphonated bitumen, N. F., accounts for the brown color. I am sorry that the specimen for biopsy was spoiled by poor fixation.

DR. H. MONTGOMERY: I believe that the clinical picture is one of lupus erythematosus. At the margins of the process where the hair has not been lost there is an erythematous raised border, and typical keratotic plugs are present.

LICHEN SCLEROSUS ET ATROPHICUS. Presented by DR. S. E. SWEITZER.

In A. H., a white woman, aged 51, the condition began two years prior to presentation as pea-sized, mildly pruritic papules over the skin in the region of the left clavicle. More of these lesions appeared in that location, as well as under the breasts and over the abdomen. In the course of a year they assumed the appearance presented. The Wassermann test was negative. Thus far therapy had consisted of the administration of arsenic trioxide in the form of pills. Biopsy was performed.

DISCUSSION

DR. JULIUS DOERFFEL (by invitation): The case presented does not seem to me to be typical of lichen sclerosis. I should rather call it scleroderma circumscripta, not only from the clinical but also from the histologic standpoint. The histologic picture lacks lymphocytic infiltrate and other features characteristic of a lichen papule. On the other hand, there is, in the section, diffuse atrophy and sclerosis. Generally speaking, we have to be very careful in making a diagnosis of lichen sclerosus, because the literature shows cases which we have to consider as intermediary between scleroderma and lichen planus. These cases are considered as morphea by some and as belonging to the lichen planus group (Gans) by others. However, I have seen recently in the Mayo clinic cases of typical lichen sclerosus et atrophicus that impressed me as being a definite entity.

DR. H. MONTGOMERY: Clinically, I should concur in the diagnosis of lichen sclerosus et atrophicus. The histologic picture was more suggestive of morphea, although it could represent an end-stage of lichen sclerosis. A patient I have seen and one recently shown in Chicago presented typical areas of localized scleroderma or morphea in addition to the areas of lichen sclerosus et atrophicus.

DR. W. H. GOECKERMAN: Lichen sclerosus et atrophicus has been of unusual interest to me in the last few years. When seen during the papular stage, particularly when the eruption is extensive, it reminds one of lichen planus without the purplish discoloration. The course of the disease is not the same as that of morphea. I have come to regard it as an entity. We probably often see it in its end-stage only. It is probably identical with lichen albus of von Zumbusch.

DR. S. F. SWEITZER: We put these conditions in two groups; one includes lichen sclerosus et atrophicus, lichen albus of Zumbusch and chronic atrophic lichenoid dermatitis of E. Csillag, and the other includes morphea, white spot disease, and cardlike scleroderma of Unna. These are all forms of scleroderma. I included my case in the first group.

DR. H. E. MICHELSON: In spite of written and informal discussion, the question of the relationship between guttate morphea and lichen atrophicus has not been clearly defined. The more one observes sections from these cases, the more one is impressed with the sclerotic processes in morphea and the fringe of infiltrate in the atrophic lichen. Furthermore, those who have lesions typical of one condition in one part of the body, have lesions in another area that might be diagnosed as the other condition. For example, in the case presented, the lesions in the clavicular region (including those on which biopsy was performed) are

typical for the lichen of Hallopeau, while nearer the waistline there are several papules that are just as characteristic for guttate morphea.

I have reviewed the records of eighty-three of my private cases of lichen planus and, although I have seen atrophic lesions in lichen planus, I have not found lesions that in any way simulated those of lichen atrophicus et sclerosus.

DR. L. H. WINER: The slides projected show the difference between lichen sclerosus et atrophicus and scleroderma. In scleroderma the entire cutis is involved, whereas in lichen sclerosus et atrophicus only the papillary and upper reticular cutis are homogenized, and this homogenized area is surrounded by a mantle of round cells infiltrating at its lower border. The microscopic differentiation between these conditions is much easier than the clinical.

DR. H. MONTGOMERY: In the early stages of lichen sclerosus there are histopathologic changes that are fairly characteristic of the disease. In the later stages, I doubt whether the pathologic picture can be distinguished from that of morphea.

DERMATITIS HERPETIFORMIS. Presented by DR. S. E. SWEITZER.

In D. B., a white girl, aged 13, the lesions appeared ten months previously with grouped vesicles over the back of the neck. In the course of about a month the disease had spread over the back and the upper extremities. The lesions consisted of papules, vesicles, excoriations and, later, pigmentation. There had been moderate improvement after the institution of therapy. The Wassermann test was negative. The treatment had consisted of autohemotherapy, from 5 to 8 cc. of whole blood being withdrawn from the vein and injected into the gluteal muscles. Modified calamine lotion had been used locally.

CARCINOMA OF PENIS. Presented by DR. H. E. MICHELSON.

O. S., a white man, aged 70, first noticed a papular lesion on the glans in January, 1931. The prepuce could be retracted. The lesion spread gradually and involved most of the glans, with partial destruction of the left portion. A partial phimosis was present. Inguinal nodes showed no clinical evidence of metastases. The Wassermann and Kahn tests of the blood were negative.

BLASTOMYCOSIS. Presented by DR. H. E. MICHELSON.

T. B., a white man, aged 28, in January, had a productive cough with blood-streaked sputum. In March, 1931, there was some loss in weight, and he had night sweats. In April, bacilli were said to have been found in the sputum (which was repeatedly negative while the patient was in a sanatorium) and there was cavitation in the right lung. The pulmonary condition had resolved almost completely with pneumothorax and rest in bed.

The eruption began as a red papule on the fingers of the left hand and gradually became generalized and ulcerated or granulomatous. Many lesions were secondary to the involvement of deeper structures; some were primary in the skin. Multiple destruction of bone was demonstrated by roentgenograms. The patient had worked in California for six months in 1930 as telegraph lineman and in a vineyard. Smears showed refractile, doubly contoured, occasionally budding, granular bodies. Culture showed budding forms, endospores and bodies of various sizes. Biopsy showed acanthosis, microscopic abscesses, plasma cells and giant cells at least one of which contained a doubly contoured body.

The treatment had consisted of potassium iodide, arsenicals given intravenously and actual cautery.

DISCUSSION

DR. H. E. MICHELSON: We have come to the conclusion that we are dealing with an extensive case of blastomycosis with internal involvement. Because all other treatment has been of no avail, I am going to administer deep diathermy over the entire body.

DR. J. BUTLER: Was sporotrichosis considered?

DR. H. MONTGOMERY: Pus obtained from a patient with systemic blastomycosis or sections of tissue will reveal typical double-contoured bodies, with reproduction by budding and never by endosporulation. In contrast, however, the cultures from these two diseases may show features of either and are not reliable criteria for differentiation. In the literature, several cases have been reported in which the generalized form of coccidioidal granuloma and systemic blastomycosis presented similar clinical features. Involvement of the bones in the case presented, the fact that the patient has been in the San Joaquin valley and the report of questionable endosporulation in the tissue sections, would point toward this being a case of coccidioidal granuloma. I believe that further studies should be made of the sections.

SYCOSIS VULGARIS. Presented by DR. H. E. MICHELSON.

In C. S., a white man, aged 47, the eruption began on the left side of the face in 1912 and spread for a period of two years. It was confined to the bearded areas, and consisted of papules and pustules with a follicular distribution on an erythematous base. Previous treatment had been unsatisfactory and had consisted of local applications, intramuscular injections, autogenous vaccines and roentgen therapy to a total of 5 skin units given in another clinic.

Recently treatment with local application of the following medication had been extremely satisfactory:

	Cc. or Gm.
Sulphurated potassium	3.75
Zinc sulphate	3.75
Water	q.s.
Salicylic acid	1.5
Phenol	1.5
Alcohol, 70% q.s. ad	180.0

DISCUSSION

DR. H. E. MICHELSON: The patient has responded very well to treatment with modified white lotion, N. F., as recommended by Prosser White.

DR. J. BUTLER: In what percentage of the cases did the condition begin on the upper lip as a result of a chronic nasal discharge? Personally, I think that in most of them the condition begins that way.

DR. W. H. GOECKERMAN: When the upper lip shows much involvement in sycosis vulgaris the nasal and paranasal structures are almost always suspected of being the cause of the infection, but the otolaryngologist can seldom be of much service in the treatment.

A CASE FOR DIAGNOSIS (ANGIOKERATOMA? LIPOIDOSIS CUTIS?). Presented by DR. H. E. MICHELSON.

M. G., a white man, aged 54, froze his fingers in December, 1930. They became red and painful, but ulceration did not occur. Later the joints of the fingers became swollen and painful on motion. This was followed by pain in both hips and other joints of the body. In April the back became painful on motion, and the fingers ached and became numb at times. In June, he first noticed red hemorrhagic areas under the skin following minor trauma. The tongue became sore and "little blisters" appeared. All of the teeth were then extracted. The lesions progressed and involved the buccal mucous membranes; hemorrhagic areas appeared and regressed. No definite keratomas followed the lesions on the fingers. There are no significant lesions on the scrotum. There is puffiness or infiltration of the eyelids. Until the fall of 1930, the patient was a cabinet maker. The Wassermann and Kahn tests of the blood were negative. The Mantoux test was

negative. Bence-Jones protein appeared persistently in the urine. The spinal fluid was normal. Roentgenograms demonstrated hypertrophic arthritis and no myelomas.

Examination of the blood showed: hemoglobin, 82 per cent; white cells, 11,100; polymorphonuclears, 66 per cent; platelets, 200,000; bleeding time, 2 minutes and 10 seconds; clotting time, 6 minutes and 30 seconds; urea nitrogen, 14.1 mg., sugar, 0.065 mg., calcium 12.7 mg. and cholesterol 168 mg. per hundred cubic centimeters. The water concentration test gave normal results; the result of the Rehberg test was 115.

Biopsy of sections from lesions of the mucous membrane showed dilated vessels and microscopic hemorrhage into the tissue. There was a peculiar homogenization of the deeper tissues. Various fat stains gave negative results. Staining of the tissue for amyloid gave negative results.

Specimens taken from lesions on fingers for biopsy showed moderate hyperkeratosis, dilatation of vessels and microscopic hemorrhage into the tissues.

DISCUSSION

DR. H. E. MICHELSON: We have been unable to arrive at a conclusion concerning this patient. The lesions on the hands resemble angiokeratoma, and the history definitely suggests this condition. The microscopic observations do not substantiate the clinical diagnosis. The lesion on the tongue is extraordinary in our experience. In all sections there is, apparently, a peculiar degeneration of the upper portion of the corium; our differential stains have not revealed what the process is. The condition of the tongue resembles lipidosis mucosae as described by Urbach. We have sent slides to Dozent Urbach for his opinion. We must keep the report of this case in the file of undiagnosed cases.

DR. H. MONTGOMERY: The histopathologic picture is not that of angiokeratoma. I believe that the condition has to do essentially with degeneration of the connective, and probably of the elastic, tissue; possibly it could be termed an atypical colloid degeneration of the skin. There is a possibility that a metabolic disturbance such as amyloidosis is also playing a rôle in the process. Whereas typical cases of colloid degeneration of the skin and pseudoxanthoma elasticum are readily distinguished both clinically and histologically, I believe that there are many cases in which the two conditions tend to merge and present all gradations and variations from the two extremes of pure elastic and pure connective tissue degeneration.

DR. L. H. WINER: We thought of the degeneration that Dr. Montgomery mentioned. We stained the tissues for amyloid but they did not take stain of any kind. We then stained the tissues for elastic tissue, and the stain was not taken. Van Gieson's stain for connective tissue was then employed and the section remained practically unstained. We then stained it with azocarmine, which Dr. E. T. Bell suggested, and we found that instead of taking the blue, as does normal connective tissue, it took a faint pink color. As yet we have no idea what the substance around the vessels is.

DR. JULIUS DOERFFEL (by invitation): The histologic picture of angiokeratoma mibelli is so typical that the diagnosis is not difficult. This case lacks the characteristic marked sinus-like dilatation of the papillary and subpapillary vessels. Furthermore, the connective tissue shows a peculiar degenerative feature which would be unusual for a case of angiokeratoma mibelli.

MULTICENTRIC BENIGN SUPERFICIAL EPITHELIOMAS. Presented by DR. H. E. MICHELSON.

Mrs. H., a white woman, presented multiple superficial ulcerated lesions on the trunk and extremities. Manipulation produced bleeding. The lesions had previously been treated with irradiation and showed telangiectasia and atrophy. Biopsy showed superficial epithelioma of the basal cell type.

DISCUSSION

DR. H. MONTGOMERY: This is a typical case of superficial epitheliomatosis. Many of the lesions also show definite roentgen and radium dermatitis; nevertheless new growths are developing in these areas. In the past I have emphasized that the lesions of superficial epitheliomatosis are often resistant to the roentgen rays and radium. This case illustrates that point. In the great majority of cases that I have seen in which radium or the roentgen rays have been employed there has been a recurrence of the lesions at the sites treated. In many instances these tumors microscopically are slow-growing basal cell epitheliomas which show little evidence of mitoses and are composed of matured and well differentiated basal cells. If roentgen rays are used in such cases, one apparently no longer has the benefit of any selective action of the rays, so that it becomes necessary to use massive dosage; the effect is fundamentally no different than if the lesions were treated with cautery. Most of the lesions in superficial epitheliomatosis are on the trunk where the skin is relatively loose, so that it is fairly simple to excise even relatively large plaques and approximate the edges of the skin without having to resort to skin grafts. I believe that these lesions should be treated with cautery or preferably by surgical excision.

DR. J. BUTLER: Would freezing the lesions with ethyl chloride, curetting them and applying trichloracetic acid be advisable?

DR. J. E. MADDEN: The roentgen treatments were given at another institution. We have treated several lesions with actual cautery. The method spoken of by Dr. Butler, "the Sherwell operation," has been used frequently in Dr. Wile's clinic, with satisfactory results.

DR. J. BUTLER: I had a case in which there were possibly thirty lesions, some as large as a quarter. At first I gave applications of radium, but I became tired of that method. I then curetted the lesions and used trichloracetic acid, and they cleared up perfectly.

DR. H. MONTGOMERY: In two cases in which treatment was given elsewhere with carbon dioxide snow there had been a recurrence of the lesion at the site treated. I have had no experience with curettage of the lesions. I have no objection, however, to treatment with snow or acids, as the lesions are usually relatively benign. It is also true that a few do respond to radiotherapy. A lesion, however, that has been inadequately treated by radiotherapy or treated to the point of radiodermatitis is just that much more difficult to remove surgically and, I believe, may also become more malignant.

DR. J. BUTLER: I did not use carbon dioxide snow; I froze the lesions with ethyl chloride.

HYPERPIGMENTATION (ARSENICAL) ASSOCIATED WITH CIRRHOSIS OF THE LIVER. Presented by DR. H. E. MICHELSON.

J. J., a white man, had noticed increased pigmentation associated with pruritus over a period of five years. There had been exacerbations and remissions. The patient was a taxidermist by trade and consequently worked with arsenic for long periods. At one time, about 1913, a diagnosis of acute arsenic intoxication was made. Examination showed evidence of recent loss of weight, enlarged liver and spleen, and icterus, as well as a diffuse hyperpigmentation. The blood pressure was normal.

Papillomatous naevus pigmentosus removed from the axillary region showed increased pigment in the basal layer of the epidermis. Prussian blue stain showed no iron.

DISCUSSION

DR. H. E. MICHELSON: The history states definitely that the patient had an acute arsenical poisoning years ago. Because of the occupation, the diagnosis of chronic arsenical poisoning may be considered. The pigmentation is more of the type which accompanies chronic dermatitis or which results from the itching of chronic jaundice.

DR. H. MONTGOMERY: The histologic sections show a palisade-like arrangement of the basal cells, pyknosis of the nuclei and increased pigmentation, which suggests the possibility of an arsenical pigmentation. There is, however, no inflammatory reaction in the cutis. I should suggest that further studies for arsenic be made by Osborne's method.

XANTHOMA DIABETICORUM. Presented by DR. H. E. MICHELSON.

W. H., a white man, aged 26, presented an eruption on the buttocks and on the extensor surfaces of all extremities, which began as yellowish papules in July, 1931. The history showed that diabetes mellitus had been present at least since May, 1931, as indicated by symptoms. This condition was uncontrolled until the patient's admission to the University Hospital in September. The blood sugar at that time was 252 mg. per hundred cubic centimeters and the cholesterol was 327 mg. Marked involution of the lesions occurred during the management of the general condition. Biopsy was done.

DISCUSSION

DR. L. H. WINER: It is interesting to note that the lesions have almost disappeared since the patient has been given antidiabetic treatment. The histologic picture showed many giant cells as well as cells full of lipoid-staining substance.

GUMMA OF THE TESTIS. Presented by DR. S. E. SWEITZER.

In a white man, aged 46, a tumor of the testis had been present for the past month, gradually increasing to its present size. There had been no pain. The Wassermann reaction was repeatedly positive. Antisyphilitic therapy has not been given. The patient states that he had primary syphilis three years ago.

DISCUSSION

DR. J. F. MADDEN: The tumor appears to be a hydrocele on transillumination. I thought that the testis was of normal size.

DR. S. E. SWEITZER: I hardly think that the hydrocele is bothering the patient at all. He is shown to demonstrate syphilis of the testis.

DR. H. E. MICHELSON: In syphilis of the epididymis, marked hydrocele may accompany the process. The hydrocele may absorb under antisyphilitic treatment. With the chronic interstitial type of syphilis of the testis, there usually is no hydrocele; the enlarged testis completely fills the scrotum on the involved side, and, as the process continues, complete atrophy may result.

PHILADELPHIA DERMATOLOGICAL SOCIETY

J. P. GUEQUIERRE, M.D., *Secretary*

Friday, Dec. 4, 1931

J. H. SCHILDKRAUT, M.D., *Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. R. GILMAN.

L. B., aged 17, entered the Philadelphia General Hospital wards a week before presentation. She had generalized urticarial dermatosis with predilection for the thorax, back and extremities. In addition there were several large, circular, punched-out ulcers with granulating bases, one on the right ear lobe and cheek, one on the nape of the neck surrounded by a group of papules, another on the right hand, one on the left arm, one on the abdomen, several on the right

arm and some on the thighs and legs. The primary lesion was apparently a papule, many of which were present about the buttocks; within a short time these lesions pustulated and then ulcerated. The ulcers were not indurated, nor was the skin about them. The bases were very tender; they did not bleed.

The patient gave a history of having had a small red itchy lump, resembling a mosquito bite, on the right thigh five weeks previous to presentation. She scratched the top off, and a little fluid oozed out. The lump then began to increase; in a week it broke down, discharged pus and left the present ulcer. The second lesion to appear was on the nape of the neck; others followed. Three weeks later, after a blood test, she was given injections into the buttocks. Seven weeks before presentation she was given powders by a physician for headache and backache. She had also used some bitter "blood medicine" made up by a druggist and Ex-lax.

The only positive observations were inguinal adenopathy, diseased tonsils and pelvic inflammatory disease.

The Wassermann test was negative. The blood count was: red cells, 3,150,000; white cells, 6,000; polymorphonuclears, 72 per cent; lymphocytes, 26 per cent, mononuclears and transitionals, 2 per cent. The urine was negative for bromides, iodides and parasites. The blood sugar was 104 mg. per hundred cubic centimeters, the urea 13. Smears were made, but no sickle cells were reported.

DISCUSSION

DR. E. F. CORSON: I think that the condition is a dermatitis medicamentosa, probably from bromides.

DR. J. F. SCHAMBERG: It is difficult to express a definite opinion of this case, because the lesions are in process of involution. I received the same impression as Dr. Corson, that, owing to the elevated, somewhat flat, vegetating lesion on the face, the condition could probably be diagnosed as an eruption following treatment with bromide.

A CASE OF ACUTE PYODERMIA. Presented by DR. R. GILMAN.

R. G., aged 7 years, a white school boy, was admitted to the Philadelphia General Hospital in September. His condition was infectious dermatitis, mainly around the calves of the legs, ankles and feet. That infection cleared up, and he was progressing nicely, when, on November 30, he had an outbreak of vesicles and pustules scattered in groups over his body, particularly in the pubic region, groin, back and neck. The lesions resembled varicella. The mucous membranes were intact and of normal color, and there was no rise of temperature. The urine was normal.

DISCUSSION

DR. V. C. GARNER: I suggest the diagnosis of hydroa puerorum originally described by Unna, and in this country by Haase and Hirschler, in about 1909. Hydroa puerorum is a condition closely allied to hydroa aestivale, but the lesions occur particularly on the trunk instead of on the exposed parts. Many believe the former is a variety of dermatitis herpetiformis. Unna believes it is a distinct entity occurring only in boys, with vesicular and bullous lesions, and at times secondary impetiginization.

DR. J. F. SCHAMBERG: The suggestion of Dr. Garner is pertinent. As I looked at some of the lesions, large, clear blebs, a little larger than the size of a pea, I thought they looked like juvenile pemphigus, particularly the type seen after vaccination. I looked at the child's arm to see whether he had had a recent vaccination. I am sure this condition belongs to the group of dermatitis herpetiformis. I am not absolutely willing to concede that hydroa puerorum is a distinct entity. There are blebs involved in hydroa puerorum, too, and a good bit of secondary pyogenic involvement, which may readily occur in children from scratching and finger infection. I think it will be found that this child will have

repeated attacks of these lesions. We know that juvenile pemphigus is a disease which is often of a few years' duration, and it is possible that juvenile pemphigus belongs more properly to the group of dermatitis herpetiformis than to that of true pemphigus; it is only a difference in nomenclature whether you call the condition dermatitis herpetiformis or hydroa puerorum. The clinical characteristics are not sufficiently definite to separate one disease from the other.

DR. JOHN H. STOKES: I agree with Dr. Gilman that this is an acute outbreak of a bullous impetiginous process, though it may turn out under observation to be one of the other possibilities that are suggested. At the last meeting of the Society I reported, in connection with a case then shown by Dr. Weidman, two patients whose condition was germane to this case. I should like to report on them. Both presented extensive bullous lesions suggesting pemphigus. The first patient, a rabbi who in conjunction with his condition presented a transient positive Wassermann test of the blood, has since died of acute febrile pemphigus. You will recall that he presented much evidence to support the belief that he had butcher's pemphigus with streptococcal or staphylococcal systemic infection. The second patient was a woman whose clinical condition at first seemed closely to resemble that of this boy. She had the marked flexural involvement and the extensive bullous eruption with scattered impetiginous manifestations which appear in this case. The woman has recovered completely under roentgen and quartz lamp therapy with dilute ammoniated mercuric ointment. If further attacks occur in this boy's case, the diagnosis of Dr. Garner and Dr. Shamberg would be substantiated. I neglected to mention that the rabbi developed a terminal cardiac lesion, apparently mitral in character, as part of his septicemia.

A CASE OF DUHRING'S DISEASE. Presented by DR. R. GILMAN.

H. H., aged 39, a colored mechanic, was admitted to the Philadelphia General Hospital with generalized, symmetrically distributed, polymorphous dermatosis, the elementary lesion of which was a wheal. The face was the only excepted area in the distribution. The lesions itched intensely, and many of the wheals were excoriated from scratching. Pustules of varying size were present in many places where the skin was excoriated, probably due to secondary infection. The condition was of five years' duration; the lesions from previous attacks had healed with hyperpigmented scars. The finger-nails, penis and scrotum were not involved. He had hypertrophied, diseased tonsils and carious teeth.

The patient said the disease began five years before presentation with itching over the sternum; lesions appeared only after scratching. He had had several attacks. His condition was aggravated by heat and sweat, and grew worse at night. Laboratory tests appeared to shed no light on the condition.

A CASE OF PRURIGO NODULARIS. Presented by DR. E. F. CORSON.

E. W., a colored girl, aged 19, had suffered from chronic cutaneous disease for five years. It began as peculiar and variously described symptoms of sensation and itching that induced considerable scratching. Afterward an eruption of pruriginous type developed, in the form of fairly discrete, firm, infiltrated nodules, mainly located on the lower part of the legs and on the forearms, although the buttocks and lower part of the abdomen were sites of lesser infection. The face and upper portion of the trunk were comparatively free from lesions. Biopsy was made two days before presentation, when she was first seen; no report has yet been made.

DISCUSSION

DR. M. BROWN: I agree with the diagnosis of prurigo nodularis.

DR. J. F. SCHAMBERG: This is a typical case of prurigo nodularis. About twenty years ago Dr. Hirschler and I reported, with microscopic studies, a case of "multiple tumors of the skin associated with itching," in a colored woman. That was before the name of prurigo nodularis was employed. The French

call this type of lesion lichen cornée or lichen obtusus; it is all one condition. It is seen in both colored and white people, and the amount of itching is often extreme. I have a woman under my care now for whom we are able to do nothing. She is violently distressed and abrades the lesions constantly. I have seen one case in which great improvement was brought about by hot baths of epsom salts and thyroid gland given internally, but such treatment was not effective in several other cases. This case is a replica of that Dr. Hirschler and I described.

A Case for Diagnosis, with Tentative Diagnosis of Lymphangioma. Presented by Dr. V. C. Garner.

A man, aged 20, presented a bony anomaly of the extremities, with gross deformities, shortening, twists and osseous tumors, which was labeled chondroplasia in the hospital. On the left leg, which was grossly deformed and elephantiasic, he presented multiple papillomatous lesions, which were grouped about the ankle in two distinct masses with a deep, ulcerated fissure between them. The numerous lymphangiectasic vessels over the surface of the skin in conjunction with the elephantiasic changes seemed to suggest a diagnosis of lymphangioma cavernosum.

According to the patient's history, this difficulty of the left leg was of only two years' duration. On puncture the superficial vesicular lesions exuded lymph, which drained for a considerable time.

This case was seen through the courtesy of Dr. Mitchell, of the surgical service of the Germantown Hospital.

DISCUSSION

Dr. V. C. Garner: I might say that although I have little knowledge of bone pathology, and little time to look it up, I am bold enough to disagree with the diagnosis of a chondroplasia. I think the bony abnormalities here conform better to the characteristics of hereditary deforming chondrodysplasia with multiple exostoses due to disturbed growth in the metaphyses of the bones.

Dr. J. F. Schamberg: I am particularly interested in this case, because I showed in my clinic today a woman, aged 31, who was only 4 feet tall. She was extremely stunted in growth, with marked curvature of the tibia; she suffered from von Recklinghausen's disease and a chondroplasia, as shown by roentgenograms of the bones, including the skull. The case was not identical with that presented, but in view of the short leg in each case and the presence of von Recklinghausen's tumors, my case is of interest. An accurate past history as to the duration of the growths on the leg and the trunk, which this patient is not able to give, would be of great value. On the upper left side of the trunk the growths may have started as soft papillomas. On the trunk the lesions are cystic, but it would take a microscopic examination to exclude malignancy. The condition may end in sarcoma. On the leg there is considerable enlargement of the lymphatic vessels with production of a lymphangioma, but of course lymphangiomas may grow where there is obstruction of circulation or occlusion of lymph vessels from various causes. It is not an ordinary elephantiasis nostras, which is due to repeated inflammation of the lymphatics, with gradual enlargement of the tissues. I think the case will have to be studied further from the pathologic standpoint before a definite diagnosis can be made of the various lesions. There seems to be some structural substratum in this case which is similar to that in the case I saw today, and which puts them on pretty much the same plane.

Dr. John H. Stokes: I can add nothing except a comment on the extraordinary character of the picture presented. I understand the patient is on a service other than the dermatologic, so that some of the studies we should have liked to make may be difficult to secure. The urine should certainly be examined for Bence-Jones protein, and a biopsy specimen of one of these nodules that move around in the skin should be obtained. I think the suggestion that Dr. Schamberg

made, that this suddenly developing, lymphangiomatous hypertrophy of the leg may be the result of internal obstruction of the lymphatic system, is well supported. The outward bulging of the umbilicus with an angiomatous-looking mass and the lymphatic obstruction of the leg, damaged by some obstructive factor, suggest some rare type of malignant development. The patient's prognathism suggests the possibility of a pituitary disturbance.

A Case of Acanthosis Nigricans Juvenilis. Presented by Dr. H. U. North.

J. C., a white woman, aged 24, presented in both axillae brown pigmented areas composed of decided epidermal thickening without induration. This hypertrophy was made up of papillary growths that were soft and velvety, except for a few warty lesions. The nails were striated and brittle, but there was no loss of hair, nor were there lesions in the mucous membrane of the mouth. She had had, however, a number of warts on the hands. The changes were first noted twelve years before presentation. Early in the course of the disease the pigmentation was considerably deeper. Under the breasts and around the neck there was a suggestion of the same condition.

The history was carefully studied, with negative results, except that prior to puberty the girl had been extremely thin; with the advent of menstruation and the development of the cutaneous eruption, she had gained considerable weight in a short period. Menstruation, though regular, had always been scant.

DISCUSSION

Dr. J. F. Schamberg: I should regard the case as beginning Darier's disease. The axillae are the typical location for Darier's disease, which is a condition much commoner than acanthosis nigricans juvenilis. I think the miscroscopic sections are also suggestive of this condition.

Dr. John H. Stokes: I agree with the diagnosis of acanthosis nigricans juvenilis. Though the condition is rare, it should not be excluded from consideration. It was disconcerting to see a plaque over the presternal region with corrugations similar to those in the axillae. The multiple small fibromatous lesions should also be noted. These do not accord with my impressions of Darier's disease.

Dr. H. U. North: I am under the impression that Darier's disease is distinctly follicular and decidedly rough. This infected area has a soft, velvety feel, as in acanthosis nigricans. The axillary region is not a favorite site for Darier's disease.

Dr. J. F. Schamberg: The microscopic sections indicate that the lesions are follicular. They show follicular hyperkeratosis. I saw a number of such cases abroad. It is my opinion that this condition would probably be classed as Darier's disease. I saw no evidence of pigment in the epidermal cells in the sections. It should be remembered, too, that acanthosis nigricans is a disease that has a prognosis which is grave. Many patients with the disease develop abdominal carcinoma, whereas this patient's health has improved in spite of the condition; she has even gained weight.

Dr. H. U. North: Five years ago at the Lankenau Hospital I did see a case of the juvenile type; after Deaver had removed the young girl's appendix, her condition almost entirely cleared up. As I understand the juvenile type of the disease, it is not fatal and not associated with carcinoma. Dr. Ludy reported a case two or three years ago and collected twenty-three instances from the literature, none of which was associated with malignancy. I understand that in the adult type about 50 per cent are associated with a malignant abdominal condition. If this condition is Darier's disease, I should think that it would have progessed further and be more widespread by now.

Dr. Frederick Summerill (by invitation): Having made the pathologic report on this case, I should like to state that the demonstrated slide shows no

suggestion of Darier's disease. I last saw a case of Darier's disease about two years ago in Colorado and made the pathologic diagnosis. In this case there is increased pigmentation up to the stratum lucidum. It is not dense pigmentation and is more easily shown in silver nitrate stained sections. I am sorry I did not bring some. The pathologic picture of this case is coincident with that of acanthosis nigricans juvenilis, with the papillary elevations, particularly marked by irregular thickening of the papillary portion of the corium, accompanied by compensatory increase in the surface stratified, squamous epithelium. There are collections of lymphocytes about some of the capillaries and some of the sweat ducts, but they are insufficient to be considered an inflammatory reaction. I believe the increase is here primarily in the papillary layer of the corium. As for the hyperkeratosis mentioned by Dr. Schamberg, there is a collection of loosely formed hyperkeratosis in the folds between the papillary elevations which might at first sight give an impression of being follicular, as in Darier's disease, but otherwise there is no comparison. This disease, pathologically as well as clinically, is a problem.

DR. M. BROWN: There is a section under the microscope that we did not have two months ago, when I presented the case of a man of 35, who had a mild case of Darier's disease.

DR. J. F. SCHAMBERG: I should regard this case clinically as Darier's disease, although the microscopic section is thick and not well adapted to careful study. Of course there are various types of Darier's disease; the axillary type is not uncommon.

NEW ENGLAND DERMATOLOGICAL SOCIETY

WILLIAM P. BOARDMAN, M.D., *Secretary*

Regular Quarterly Meeting, Dec. 9, 1931

ARTHUR M. GREENWOOD, M.D., *Presiding*

LUPUS ERYTHEMATOSUS. Presented by DR. W. P. BOARDMAN.

J. S., an American housewife, was admitted to the skin department of the Boston City Hospital for an eruption on the face and scalp of nine years' duration. It started on the left nasal fold and spread gradually until the whole left cheek was involved, and later the right cheek and the scalp. The lesions were sharply circumscribed, scaling and ulcerated, and there were eroded areas with patches of scarring. The follicles were enlarged.

Five weekly doses of gold and sodium thiosulphate, 0.005 Gm. each, were given with considerable improvement.

DISCUSSION

DR. H. P. TOWLE: I should like to ask if you think all the lesions are lupus erythematosus? They are rather acute and extensive. It seemed to me that there was a tuberculous element to be considered.

DR. C. G. LANE: The thing that struck me in this case was the type of scarring. Certainly areas on the forehead warranted a suspicion that the patient had had radiation therapy. She had had no roentgen treatment so far as I could find out. I think there is a lesson for us so far as radiation treatment of lupus erythematosus is concerned. The end-results of lupus erythematosus and the end-result of over-radiation are so much the same that one should at least use extreme care in the treatment of lupus erythematosus by radiotherapy.

DR. J. W. LANE: I should ask if you do not think that radiation therapy makes the condition worse unless given in very small doses?

DR. C. G. LANE: Yes, I think so.

DR. A. M. GREENWOOD: I thought that the cheek was very florid for lupus erythematosus.

DR. BERNARD APPEL: Apropos of the marked improvement under such apparently small doses, I should like to state that it seems to me that the tendency is to give smaller and smaller doses of compound gold, as more and more reactions are being reported from the use of large doses.

DR. A. BLUMENFELD: I have been using gold and sodium thiosulphate locally for lupus erythematosus according to Traub's and Monash's suggestions. I use 15 mg. in one local area. The immediate reaction is one of marked swelling; the area became swollen and very pendulous, and even with the concomitant anesthesia the reaction lasted twenty-two hours, but the results so far were very good. In six treatments the lesions have almost disappeared. The reaction in these cases was entirely local.

DERMATITIS MEDICAMENTOSA (PHENOLPHTHALEIN). Presented by DR. F. P. MCCARTHY.

I. P., an American housewife, aged 54, has an eruption on the face and hands. The first attack occurred about two years before presentation. An eruption developed on the right cheek and dorsum of both hands with large blister formation. On Feb. 9, 1931, when the patient was first seen, there was a large, violaceous, pigmented lesion on the dorsum of the right hand with a flaccid, bullous lesion superimposed. The lesion occurred in the same location as the one in her previous attack. On Dec. 1, 1931, she was seen with a similar eruption on the right cheek and the dorsum of the right hand, with several macular and bullous lesions of the left hand and wrist. She gave a history of the ingestion of two phenolax wafers and one-half an Ex-lax wafer. The eruption developed the day following the ingestion of the cathartic. She remembers that at one of the previous attacks she also took phenolax. The lesions caused considerable burning with moderate itching.

In the right cheek there was a circular, violaceous macule with an epidermal bullous lesion, the contents of which had been emptied. This lesion was about the size of a quarter and corresponded in location with the lesion of the former attacks. On the dorsum of the right hand was a large circular, violaceous macule about the size of a half dollar without the bullous change. On the dorsum of the left hand and on the external aspect of the left wrist were several similar violaceous, macular bullous lesions.

DISCUSSION

DR. F. P. MCCARTHY: I might add that the patient made the diagnosis in this case. My first reaction was that the condition was erythema multiforme, but on the last visit she spoke of the ingestion of phenolphthalein.

DR. C. G. LANE: The striking thing about this case is the connection between the bullous and the macular lesions. I do not know that I have ever seen an acute bullous type such as occurred here. I remember well a case of phenolphthalein dermatitis that I watched. The patient came in with a story very suggestive of blood eruption. She said that she had been taking two things, a cough medicine thought to contain iodine and laxatives which suggested phenolphthalein. I left an order for the patient to be given a 0.5 Gm. of phenolphthalein as a test. She was given 1 Gm. and had a most uncomfortable night. She was awakened with intense burning and itching, and before the night was over she had to have two hypodermics of morphine to quiet her. Her body was covered with a purplish red rash which was very widespread and uncomfortable, and which persisted. Since then I have been very careful about dosage in such cases.

DR. J. W. LANE: These cases persist a long time. In the last case I saw the patient was almost covered from the neck down and had not had a dose of phenolphthalein for six months; the itching and burning was intense even then.

The patient had it six months before finding out what the trouble was. About the bullous eruptions, that is not very common. I have seen one or two cases.

DR. A. BLUMENFELD: At times it seems as if one gets very diversified eruptions from phenolphthalein. Dr. Mitchell speaks of the lichen spinulosis reaction of phenolphthalein which corresponds to many lichen spinulosis eruptions due to alleged fungi.

DR. J. H. BLAISDELL: I feel reluctant to accept offhand a diagnosis of eruption due to phenolphthalein. The history I obtained from this woman was that on Thanksgiving Day the skin was normal, and within forty-eight hours the area on the back of the right hand progressed from erythema to vesiculation and has since dried up. I think this healed as well as you would expect any severe bullous eruption on the back of the hand to do. I would suggest possibly an artefact.

DR. F. P. MCCARTHY: To rule against that diagnosis, I would cite the lesion on the face which persists in its pigmentation even between the attacks, and the lesion on the right hand also had a pigmented area prior to this last attack which had not entirely cleared up. The lesions have always come out in the same places, suggesting areas of lowered resistance. The fact that Dr. Lane knows of cases of the bullous type, and that these bullous lesions are consistent with those due to phenolphthalein, that there is a clear history of the patient taking two phenolax wafers and one-half an Ex-lax wafer the night before the eruption and that she had a burning sensation, to me rather clinch the picture of a phenolphthalein reaction. The patient is the type of woman who certainly would not tend to produce a factitial lesion for the sake of sympathy. So, even though the locations are such that they could possibly be produced by the patient, that particular thing did not come into my mind.

DR. J. W. LANE: Would not that amount of irritation be almost unknown in such a case?

DR. J. H. BLAISDELL: I simply took the patient's statement that the skin was entirely clear before the eruption. Was the phenolphthalein taken between the attacks?

DR. F. P. MCCARTHY: Yes, and this has happened three times.

DR. J. W. LANE: The location on the hand is rather unusual in my experience. It looks to me very typical, however.

DR. BERNARD APPEL: I had a patient on whom a diagnosis of bullous erythema and pemphigus was made. He had several attacks, which always came on after taking a coal tar preparation for migraine. He stopped taking the drugs and was free from lesions for a long time; then one night he had an unusually severe attack of migraine, and feeling worn out with his suffering, took some of a coal tar preparation — in this case, Amidol — and another attack of the bullous eruptions promptly developed. There was a question also of his having taken some phenacetin. I imagine that all coal tar preparations contain some phenol, which is the cause of the toxic eruptions.

URTICARIA PIGMENTOSA WITH PURPURA. Presented by DR. LORETTA J. CUMMINS.

S. R., a 3 year old boy, white, was admitted to the Children's Hospital. There was a history of seborrheic eczema when the child was 7 weeks old. The present eruption began in October, 1931, and has persisted. There are several pea-sized, buff-colored, nonelevated lesions on the body. There is no itching and no urticarial reaction. The boy had several hemorrhagic lesions on November 20, and a temperature of 100 F.

Blood smears showed: platelets, normal; polymorphonuclears, 40; eosinophils, 2; lymphocytes, 60; basophils, 0; red cells, normal in size and shape; clotting time, two and one-half minutes; bleeding time, three minutes; red cell count, 3,740,000, and white cell count, 8,000.

DISCUSSION

DR. LORETTA J. CUMMINS: I have nothing to add. I should be very glad if any of the members who saw the case can add anything to it. The child has bad tonsils, but the doctors in the Children's Hospital did not think they were very bad. However, they are going to remove them. The purpuric lesions are increasing. At first they were just buff-colored lesions which were characteristic of the urticaria pigmentosa.

DR. J. W. LANE: I do not know enough about such conditions in children to have any opinion concerning them, but in an adult I would be apt to class such a condition as an idiopathic purpura. An enormous amount of eruption can be present without the patient being apparently ill and with the blood remaining normal.

DR. BERNARD APPEL: Has this child had any calcium for treatment?

DR. LORETTA J. CUMMINS: Yes, I gave him calcium lactate about three weeks ago. The lesions are developing all the time.

GRANULOMA ANNULARE. Presented by DR. BERNARD APPEL.

N. T., white, an American, aged 21, a purser, has an eruption on his left hand of eighteen months' duration. It developed as a small red area with a smooth and shiny darker red spot in the center. It slowly grew to its present size. About eight months after onset, the area slowly broke up into one larger lesion and a small group of three small lesions on the ulnar side of the larger one. The morphology of all the lesions is identical, except that the larger one is more distinct; it has a border the outer edge of which is just within the entire red area; it is about 2 mm. wide, slightly raised, flat topped, pale, smooth and shiny. The center is flat and dull red with a loss of the normal skin markings but no ulceration.

Roentgen treatment was given.

DISCUSSION

DR. H. P. TOWLE: I should like to ask what is Dr. Lane's experience with roentgen treatment in granuloma annulare.

DR. C. G. LANE: The lesions usually respond very well. I do not think it is unusual to take three or four near erythema doses to get rid of them. I think they do a little better with nine tenths of an erythema dose. I have had them respond very well. I used an unfiltered radiation at first, but now I use one or two with the filter and the lesions react a little better. I use 1 mm. at 8 inches (20.32 cm.) distance, and give them seven eighths of an erythema dose to start with.

DR. A. M. GREENWOOD: There seems to me to be a tendency toward development of new blood vessels.

DR. W. P. BOARDMAN: I should like to ask Dr. Lane if he has seen many recurrences after his roentgen treatment.

DR. C. G. LANE: Yes, I have seen some, and I think I am apt to carry the treatment a little bit further than I did before, if too much has not been given.

PAPULONECROTIC TUBERCULIDS. Presented by DR. J. L. GRUND.

G. S., aged 43, married, out of work, has four children who are living and well. The family history was unimportant. The patient had a primary syphilitic lesion of the penis in 1907. He was treated intensively with mercury for six months. In 1915, "sores" developed on both forearms, evidently gummas. They disappeared after a number of intravenous injections of arsphenamine administered by a local surgeon. The Wassermann reaction of the blood was negative.

The patient stated that in 1922 he began to show intermittent swellings of the lobes of both ears, evidently attacks of lupus pernio. In 1926, he entered one of the local clinics for "sores" which developed on the lobes of the ears. These

had developed during the preceding year. The attacks of swelling were of a seasonal nature, coming in January, February and March. Local ultraviolet ray exposures were given. During the exposures, a crop of small papules developed on the scalp; they later ulcerated, some healing, others remaining, and new ones appearing from time to time. The patient was treated for about seven months with ultraviolet light with improvement of the lupus pernio of the ears. However, new papulonecrotic lesions appeared on the neck. The patient then discontinued treatment.

He returned to the clinic about a year ago with new lesions on the face and forearms. Because of his syphilitic history, although the Wassermann reaction was negative, he received antisyphilitic treatment for about a year. He then entered the skin clinic of the Massachusetts Memorial Hospital about Sept. 1, 1931.

On examination, he presented a number of pin-head to pea-sized papules, both ulcerated, on the scalp, the right cheek and the extensor surfaces of both forearms. Many of the papules presented necrotic centers. The lobes of both ears were "chewed away," and scarring was present. On the back of the neck were a number of papulonecrotic lesions. On the right forearms were two large scars, the sites of the old gummas. The Wassermann, Kahn and Hinton reactions were negative.

The patient received four injections of bismuth from September 1, to October 1, with no apparent improvement. On the assumption that the lesions were tuberculids, gold and sodium thiosulphate, 0.05 Gm., was administered. With the third treatment, the lesions showed signs of involution. With the seventh, remarkable improvement was apparent. Many lesions, especially those on the scalp, face and neck, had disappeared; those on the forearms were no longer ulcerated, depressed, pigmented scars having taken the place of the active ulcerations.

DISCUSSION

DR. A. W. CHEEVER: It seemed very definite that there were two separate conditions in this case. I believe that many of the scars were due to syphilis, owing to the depth and size and distribution, but some of the more recent scars were due to the process that is going on now.

DR. BERNARD APPEL: I believe we ought to mention the fact that the man responded most extraordinarily to very small doses of gold compound. He has a definite history of syphilis. The large scars, as Dr. Cheever says, are undoubtedly from syphilis, but his blood has given a negative reaction for a long time, and in spite of that the lesions have continued. Even with a negative reaction of the blood, the patient has been having antisyphilitic treatment, with no effect on the process in these small lesions. He has had iodine, arsphenamine and bismuth. In this case there was absolutely no effect. We started on very small doses of gold and sodium thiosulphate, 50 mg., and the result was quite extraordinary in a short time.

ARGYRIA? Presented by DR. LORETTA J. CUMMINS.

C. M., 3 years old, white, American, female, was admitted to the Children's Hospital. For two years the mother has noticed an increasing grayish discoloration of the skin of the body starting around the neck. At the present time the discoloration is diffuse with an occasional small clear area of normal skin on the neck. There is no history of any internal or external remedies before or since the appearance of the discoloration. No treatment was given.

DISCUSSION

DR. A. M. GREENWOOD: Was there any history of the administration of a silver compound?

DR. LORETTA J. CUMMINS: There was no history of internal or external medication, with the exception of hydrogen dioxide.

DR. F. P. MCCARTHY: I would suggest a nevus of the melanotic type as a diagnosis.

DR. A. M. GREENWOOD: Has the case been seen long enough to know whether the condition is spreading?

DR. LORETTA J. CUMMINS: I have seen the patient twice in the last two months. The mother thinks the discoloration is breaking up because the areas in the back are growing paler. The father told me very definitely that he thinks it is progressing and that the color is darker. I could obtain no history from either the mother or father that the child had taken any medicine, drops or mild silver protein had been used. The only thing the mother said was that the child had put a thermometer into its mouth, but no drugs had been given and nothing had been applied to the skin except hydrogen dioxide. Dr. White suggested that there might have been some bottle or cup that the child had been persistently drinking from. I asked them about that, but they said the child had never had anything different from the rest of the family.

DR. A. W. CHEEVER: It seemed to me that the distribution is against the diagnosis of argyria, as it does not markedly increase in the areas exposed to the light. There was a case shown here from the Beth Israel Hospital in which there was very dark pigmentation on the face and hands, but practically none on the trunk. I have seen several cases that showed this peculiarity.

DR. W. P. BOARDMAN: Isn't there usually some pigmentation of the mucous membrane in these cases?

DR. A. W. CHEEVER: Yes. I think that would be very much against the diagnosis.

DR. J. H. SWARTZ: I should like to ask if there have been any symptoms of suprarenal disease or functions?

DR. LORETTA J. CUMMINS: I think not. The child had been perfectly well, and this condition did not disturb the mother until the child was old enough to go out and comments were made about it. That caused her to take the child to the hospital. She said that the child had always been well.

DR. H. P. TOWLE: Was the child exposed to the sun, in summer especially?

DR. LORETTA J. CUMMINS: I do not know that it was.

DR. J. W. LANE: To me this is the most interesting case shown this afternoon, and the suggestion of nevus is very interesting. We would probably have a fair chance of deciding that by biopsy. The color did not look exactly like that produced by silver compound, but more like that produced by arsenic. As for Addison's disease, I do not know enough about children to know whether it occurs at that age, but I am sure that with as much pigmentation as this child has, if the condition were Addison's disease, the child would not be running around as it is.

DR. A. M. GREENWOOD: Would it be possible to have a report later?

DR. LORETTA J. CUMMINS: I do not think we are going to get much cooperation. The father has forbidden having anything further done, and the mother told me he had decided to take the child to a beauty specialist, thinking they could give him a bleach.

SYPHILITIC PAROXYSMAL HEMOGLOBINURIA. Presented by DR. R. P. MCCARTHY.

C. W., an American Negro, aged 23, cook and dental student, was admitted to the skin department of the Boston City Hospital with a history of intermittent attacks of "bloody urine" for the past two years. Each attack begins with sensations of numbness and tingling in the chest and back, followed by chilly sensations or definite chills and fever, then a strong desire to void, and the passage of red urine two or three times, after which the urine is clear. Paroxysms follow exposure to cold or when chilled and occur all through the year. The patient had a primary chancre at the age of 17. No secondary lesions were noted. Six injections of neoarsphenamine given at Camp Devens last year and eight this year were the only previous treatment.

Physical examination gave essentially negative results.

The Wassermann and Kahn tests were positive. The Donath and Landsteiner phenomenon (blood serum) were positive. The Rosenbach test was positive (hemoglobinuria following immersion of feet in iced water for 15 minutes). The urine was normal, except during paroxysm, when hemoglobin and furred cells were present.

The patient is now under antisyphilitic treatment.

DISCUSSION

DR. F. P. MCCARTHY: I should like the house officer, Dr. Wilson, who has worked up the laboratory technic in this case, to demonstrate the reaction in the blood serum.

DR. R. WILSON, JR.: (Dr. Wilson showed six glass tubes). This first tube, which shows the patient's urine before the test, is perfectly clear; his feet were then immersed in ice water for fifteen minutes, and a few hours later he passed this red urine which showed considerable hemoglobinuria and a few red cells, consistent with the diagnosis. A further test brings out the presence of isohemolysins and autohemolysins in the blood stream.

Paroxysmal hemoglobinuria is a constitutional disease rather than a kidney disease, in which group it has sometimes been classified. It is always associated with syphilis, and is due to the presence in the blood serum of isohemolysins and autohemolysins. The latter bodies may be separated from those that give the positive Wassermann reaction of the blood, and are entirely distinct. One feature that recently occurred to me is that perhaps in the small percentage of cases in which the Wassermann reaction is not positive, the hemolysis which would give a negative reading of the test might be due, not to the absence of the specific antibody, but to the presence of the isohemolysin; if the latter had been separated out previous to the performance of the test, possibly those cases, too, would have shown positive serology.

DR. F. P. MCCARTHY: In connection with this case I am treating at present a 5 year old child for congenital syphilis. The diagnosis was not made until last May. According to the history, the child had been passing bloody urine since 19 months of age, and I did not find it out until I had treated him for three months.

We took the blood and found that it gave a positive reaction. This is the second case of hemoglobinuria, both patients being under treatment at the same time. The Negro, who is in the hospital, contracted the disease about six or seven years ago. He had had six doses of neoarsphenamine prior to entrance to clinic. The incidence of this disease so soon after the primary lesion is unusual. Most cases occur fairly late. The incidence in congenital syphilis is much more frequent, and the child, since he has been getting treatment, has had no attacks of paroxysmal hemoglobinuria in spite of his exposure to cold.

Yesterday we immersed the child's feet in ice water for fifteen minutes; he was then to go home, and the mother was to save the urine so we could see if hemoglobinuria would be produced. Subsequent examination of the urine was negative for hemoglobin.

This seems to me one of the most remarkable types of serologic reactions, in which cold is the only factor that precipitates hemoglobinuria.

In this particular case we gave the patient, experimentally, a small dose of typhoid vaccine intravenously and produced a chill and fever; next we gave him a nonspecific milk preparation with negative results. Up to a few years ago the number of cases reported in the literature was about 300. I have no doubt we have cases with autohemolysins in which there are no paroxysms of hemoglobinuria, and this suggests trying this particular test in a series of syphilitic persons to determine just what percentage have the Donath-Landsteiner reaction in the blood and do not have hemoglobinuria.

DR. A. W. CHEEVER: We recently had a family at the Boston Dispensary of that type. One member had the hemolysis reaction in the blood, but there was no history of his ever having had hemoglobinuria. That will be reported later.

DR. F. P. MCCARTHY: I would suggest that we might try to find out what blood group these two patients are in, and also to find out whether Dr. Cheever's patients might be confined to a certain group.

Hemoglobinuria usually results in a pronounced secondary anemia. This child was kept constantly anemic on account of the frequency of the paroxysms.

FOUR CITIES DERMATOLOGICAL SOCIETY (CINCINNATI, CLEVELAND, DETROIT AND PITTSBURGH)

J. R. DRIVER, M.D., *Reporter*

Regular Annual Meeting, Cleveland, Dec. 10, 1931

H. J. PARKHURST, M.D., *Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. C. J. SHEPARD, Columbus.

A white woman, aged 40, developed a small white lesion on the tongue about two years before presentation, which resembled a patch of leukoplakia. It increased and new, tender and sensitive lesions subsequently appeared both on the tongue and on the buccal mucosa. About four months later a "fever blister" appeared on the lower lip which rapidly covered the whole lip with a thick crust with a raw, bleeding underlying surface. This condition slowly subsided, but the gums and tongue still show some inflammation. During this time, probably ten or twelve glistening papular lesions appeared on the feet and hands, with a thickening of the nails of both big toes. Smears from the mouth were negative for Vincent's angina and Monilia infection. Pernicious anemia was suspected but examinations of the blood gave negative results. Biopsy was performed on a section of skin and subcutaneous tissue. The epidermis was thickened, the keratohyaline layer increased and the rete pegs elongated. The dermal papillae were markedly enlarged and elongated, and throughout the upper layers of the dermis there were extensive lymphocytic infiltration, numerous plasma cells and very few leukocytes or eosinophils. There was proliferation of connective tissue and endothelial cells. In the lower layers of the dermis, the coil glands were practically normal.

DISCUSSION

DR. UDO J. WILE, Ann Arbor: I am somewhat at a loss to explain all the lesions on the patient. The lesions on the leg do not look like or seem to have the remotest resemblance to those in the mouth. The lesions on the gum and on the tongue make one think of some deficiency disease. The tongue looked like that seen in pernicious anemia, but Dr. Shepard told us that the patient does not have pernicious anemia and apparently no deficiency disease.

DR. H. N. COLE, Cleveland: I thought that this was an interesting case. The lesions on the lip, with their peculiar sort of a scaly, somewhat reddish white appearance, and also some of the lesions on the mucous membrane and a few of the lesions distributed over the lower limbs were like those usually seen in disseminated lupus erythematosus.

DR. ROBERT C. JAMIESON, Detroit: Within the last six or eight months I have had the opportunity of seeing two cases of lupus erythematosus disseminatus. I think that the picture presented by these lesions could easily fit in with the appearance of those two cases, and I should like to agree with the diagnosis advanced.

DR. LESTER HOLLANDER, Pittsburgh: I agree with the previous speakers that the diagnosis in this particular case is difficult, but I consider the possibility of the mucous membrane disturbance to be most likely associated with pernicious

anemia. The soreness of the mouth, the atrophy of the tongue and the fact that the patient is taking hydrochloric acid by mouth on account of hypochlorhydria are significant and corroborating evidences of this possibility. In addition, thrush and lupus erythematosus of the subacute variety must be borne in mind. I advise the addition of liver to the diet.

DR. MARION B. SULZBERGER, New York: Another possibility is lichen planus, particularly in view of the histologic picture. Then either a diagnosis such as ringworm or an infection of that nature, must be made to explain the condition of the toe-nails, or the condition should be considered atypical bullous or vesicular lichen planus.

DR. KARL G. ZWICK, Cincinnati: The reticulate lesion on the buccal surface of the oral cavity, together with the history, would make one think of lichen planus. If, however, one considers the condition on the toe, which constitutes a separate and distinct entity, I should venture a diagnosis of ringworm. In other words, I am inclined to believe that in this patient two conditions are present.

DR. E. W. NETHERTON, Cleveland: I thought that the condition was lichen planus, and the histologic picture appeared typical. I recall a case that Dr. Cole presented about two years ago in which the reddish lesions on the mucous membrane of the mouth and of the vagina were practically exact duplicates of the buccal lesions in this patient. I also tried to rule out the possibility of a deficiency disease. I believe the condition is a lichen planus.

DR. R. E. BARNEY, Cleveland: There were definite lesions on the tongue that were typical of lichen planus.

PROBABLE LYMPHOBLASTOMA. Presented by DR. COLE and DR. DRIVER, Cleveland.

In E. F. H., a white man, aged 50, an eruption on the forearms had appeared three years before presentation which spread to the legs and later spread over the body. The process is pruritic and of late has been scaling a great deal. For the past few months he has noticed an enlargement of all of his glands. Physical examination showed a generalized, exfoliating type of dermatitis, with hard, discrete, enlarged glands in the groins and axillary spaces and under the jaws, postcervically and cubitally. The spleen and the liver were just palpable. There were 8,000 white cells, 4,700,000 red cells and 80 per cent hemoglobin. The differential count showed: polymorphonuclears, 66 per cent; small mononuclears, 19 per cent; large mononuclears, 6 per cent; eosinophils, none, and transitionals, 9 per cent.

A gland was removed from the groin and was reported by the pathology department to show hyperplastic tuberculosis. A specimen of skin removed from one flank showed an extensive edema of the upper portion of the corium and, to a certain extent, of the epidermis. There was a notable cellular infiltration around all the vessels, and in the upper corium there were dense clumps of cellular infiltrate, made up mostly of mononuclear cells and endothelial cells, with a sprinkling of giant cells here and there. Much of the tissue in this portion was edematous. One would hesitate to say as yet that the cellular infiltrate shows a homogenous type of cell or that it resembles tuberculosis.

The patient's glands have been treated with roentgen rays, and he has received arsenic internally, with little effect as yet.

HODGKIN'S DISEASE. Presented by DR. J. V. AMBLER.

H. F., a white man, aged 24, from the service of Dr. Cole and Dr. Driver at Lakeside Hospital, who was presented before the Cleveland Dermatological Society, Oct. 29, 1931, first noticed a severe itching of the skin two years before presentation. He states that the first attack of pruritus occurred at night, awakening him from a sound sleep. Since that time pruritus over the entire body has persisted and becomes more severe at varying times. He has been seen

by numerous physicians without relief from pruritus being obtained. He has been followed at the Lakeside Hospital Dispensary since May, 1930. At this time the only positive findings were the white blood count of 14,300, with 91 per cent polymorphonuclears and deep scratch marks over the entire surface of the body. In April, 1931, several small lymph glands were palpable in the inguinal and cervical regions, and evidence of mediastinal involvement was demonstrated by physical and roentgen examination. Biopsy of a cervical lymph node showed Hodgkin's disease. Since then the patient has received six injections of antimony and potassium tartrate, followed by frequent and regular courses of deep roentgen therapy administered to the mediastinal and superficial lymph nodes. After a transitory improvement following roentgen therapy, the patient's condition has been progressively worse.

Physical examination revealed a poorly developed and poorly nourished young, white man who was dyspneic. The skin was pale, warm and moist, and practically the whole body, with the exception of the head, was covered with scattered excoriations. There was subcutaneous edema over the chest and upper part of the abdomen. The right eye was artificial. The cervical and axillary lymph nodes were markedly enlarged, discrete, firm and slightly tender. Under the right pectoral muscles there was a movable mass about the size of an orange. On percussion there was a marked widening of the mediastinal dulness and evidence of fluid in the right side of the chest. The urine showed numerous fine granular casts, otherwise it was normal. The blood count showed: white cells, 16,800; red cells, 4,900,000, and hemoglobin, 78 per cent. The differential count showed: polymorphonuclears, 90 per cent; lymphocytes, 4 per cent; mononuclears, 3 per cent, and eosinophils, 3 per cent. The Wassermann test of the blood was negative. Examination of the spinal fluid gave negative results. The basal metabolic rate was normal. Tests with tuberculin gave negative results in a dilution of 1 : 10,000. A roentgenogram of the chest showed the middle shadow markedly increased in width, the trachea displaced to the right and hydrothorax on the right side.

LEUKEMIA CUTIS RESEMBLING HERPES ZOSTER. Presented by DR. R. E. BARNEY, Cleveland.

C. A., a white man, aged 66, was first seen on Feb. 11, 1931, complaining of difficulty in walking, weakness and swellings in the neck and axillae. The difficulty in gait is due to a footdrop associated with muscular dystrophy. Progressive weakness beginning a year and a half before presentation brought him to the hospital. Two years previously a small swelling was noted under the right jaw. Subsequently, tumor masses developed in the left side of the neck and in both axillae. The eruption over the right side of the chest began about six months before presentation; a slight tingling sensation was associated with it. A blood count on Feb. 11, 1931, revealed 290,000 white cells, 90 per cent of which were lymphocytes. The patient had been under roentgenotherapy since February, 1931. On Nov. 5, 1931, he was admitted to the hospital for control of nasal hemorrhages. The Wassermann test of the blood was negative. Physical examination showed a pale, fairly well nourished man of 66. The left pupil was slightly larger than the right, owing to lymph glands in the neck, but both pupils reacted promptly to light and in accommodation. The buccal mucous membrane was pale. There were numerous carious teeth. The vermilion border of the lower lip revealed three small, pea-sized erosions. The spleen and liver were palpable. There was a bilateral footdrop. There was marked cervical and axillary adenitis. A papular eruption involved the right side of the chest, following the courses of the ninth and tenth intercostal nerves. The individual lesions consisted of yellow, dull, infiltrated, painless, nonflammatory nodules varying in size from that of a glass pinhead to that of a large pea. Biopsy of a specimen taken from one of the nodules revealed a practically normal epidermis. In the corium there was a focal infiltration with round cells, especially around the vessels. The infiltration was not monocellular, but the

majority of the cells were lymphocytes. In several areas there were clusters of large epitheloid cells with abundant cytoplasm and large pale nuclei with definite multinucleated giant cells of the foreign body type. A few mitoses were present. Only one tissue eosinophil was present in the section. Around one of these cellular infiltrates there was a small interstitial hemorrhage.

LYMPHOBLASTOMA-LYMPHOSARCOMA? Presented by DR. COLE and DR. DRIVER, Cleveland.

Mrs. A. R. N., a white woman, aged 54, was first seen in September, 1930; she had had lumps on the forehead for about three months. There was a certain amount of local pruritis. The patient had also noticed a small, hard lesion on the right cheek which had been present for some time and a red spot on the right side of the neck for about three months. The family history was essentially unimportant. She had had frequent colds and tonsillitis, and otitis media eighteen years prior to presentation, and in 1924 one tooth was removed because of root absorption. In June, 1924, she had had pyelitis.

Over the central portion of the forehead there was an area half the size of a palm showing a light, reddish color, with little induration; along the lower border of this area were three raised, rather indurated nodules, the size of castor beans. There was a similar pea-sized, dull red papule on the right cheek, and a lesion on the right side of the neck, the size of a lima bean. The glands showed nothing remarkable. The test with tuberculin gave negative results. The Wassermann test of the blood was negative. Roentgenograms of the teeth and chest showed nothing abnormal. A blood count showed: 4,424,000 red cells, 5,700 white cells and 75 per cent hemoglobin; a differential count: polymorphonuclears, 58 per cent; large mononuclears, 12 per cent; small mononuclears, 26 per cent; eosinophils, 2 per cent, and transitionals, 1 per cent. Biopsy on a specimen from one of the tumors showed a low epidermis with a slight amount of dilatation of the vessels and papillae. Distributed through the entire corium, even deep down and especially around the vessels and along the course of the smooth muscle fibers, there was an extensive cellular infiltration, almost uniformly made up of small mononuclear elements and of larger mononuclear cells with small nuclei. There seemed to be no eosinophils or plasma cells. There was possibly an increase in the collagenous element in the corium, especially in one deeper area of infiltration where a dense cellular infiltration was found. There seemed to be an absence of sweat glands.

The cellular infiltration was not multiform enough in type to correspond with that of mycosis fungoides. It resembled rather the picture one would expect to find in lymphosarcoma.

The patient has been under observation from September, 1930, until the present. She has received arsenic internally and local treatment with roentgen rays. It is remarkable how rapidly the tumors respond to a light dose of screened x-rays, only to recur, however. The lesions have spread over the cheeks, and sharply defined lesions have also appeared over the chest and over the upper portion of the back. They are usually rather firm and somewhat raised, and occasionally one notes a tendency for them to be rather arciform.

DISCUSSION ON PAPERS OF DRS. COLE AND DRIVER, AMBLER AND BARNEY

DR. UDO J. WILE, Ann Arbor: I am much interested in this group of cases and believe that the diagnosis is entirely correct in all of the cases shown. In the case of lymphoblastoma presented by Drs. Cole and Driver, I do not believe that the observation of the tuberculous architecture in a lymph gland in any way invalidates the diagnosis of a lymphoblastoma, since a tuberculous architecture is commonly seen in Hodgkin's disease.

In Dr. Barney's case, which is interesting, I believe that the patient had herpes zoster, which is of course not uncommon in leukemia, and that in the scars in the old zoster lesion there were metastatic lesions of the leukemia. In

the case of lymphoblastoma-lymphosarcoma, I should suggest the possibility of a Spiegler-Fendt type of sarcoid.

Dr. S. W. Becker, Chicago: It is possible that the herpes zoster in Dr. Barney's case was due to infiltration of the posterior root ganglions, which often occurs in leukemia. In the patient presenting the lesions on the face and shoulders (lymphoblastoma-lymphosarcoma?), the lesions were typical of leukemia or pseudoleukemia, but histologically the cells were not infiltrating the tissue to the extent which is usually seen.

Dr. Karl G. Zwick, Cincinnati: In the interest of a more exact terminology, would it not perhaps be advisable in connection with Dr. Barney's case to speak of a zosteriform distribution, rather than of a "zoster"? I feel that this is not simply or solely a matter of nomenclature, because dermatologic designations are intended to represent, as much as possible, distinct etiologic concepts.

Dr. J. R. Driver, Cleveland: The pathologic diagnosis in the case of probable lymphoblastoma was hyperplastic tuberculosis. Many pathologists are of the opinion that tuberculosis can produce a clinical picture undistinguished from Hodgkin's disease. Many years ago Sternberg and his co-workers believed that two thirds of their cases of Hodgkin's disease were due to tuberculosis; the work of Dorothy Reed which followed had the effect of throwing doubt on the interpretations of Sternberg. I am wondering whether the pendulum is not swinging back and that the importance of tuberculosis in this disease syndrome is being more clearly proved. Recently L'Esperance (*J. Immunol.* **15**:123 [March] 1928) carried out a series of experiments in which Hodgkin's nodes were injected into chickens. An avian tuberculosis developed, which clinically resembled Hodgkin's disease. We hope that we can get additional pathologic material for inoculations into animals in the further study of this case.

Dr. Marion B. Sulzberger, New York: Regarding the case of herpes zoster in the "lymphoblastoma," I think that the theory that Dr. Wile advanced is true, at least in some cases. It is well known that herpes zoster occurs much more frequently in leukemias than in other diseases of the skin On this account it is well to perform blood counts in herpes zoster whenever it is possible. With reference to the case of lymphoblastoma-lymphosarcoma, I thought that clinically it had the appearance of a sarcoid and that it might be interesting to see what the quantitative tuberculin test would show and whether there is involvement of the bones such as one sometimes sees accompanying sarcoids of the skin. In such cases one expects a relatively negative reaction to tuberculin owing to a specific hyposensitiveness of the skin.

Dr. H. N. Cole, Cleveland: With reference to the case of lymphoblastoma-lymphosarcoma, when we first saw the patient she had two or three small tumors on the forehead, and the first condition we thought of was sarcoid. But the tumors continued to appear rapidly; often a new lesion would appear in a week. This fact, taken together with the histologic appearance of the lymph glands and the remarkable reaction to the roentgen rays, made us think of a lymphosarcoma. Tests with tuberculin were negative for tuberculosis, and x-ray pictures of the lungs have shown no pathologic process.

Dr. R. E. Barney, Cleveland: In the case of leukemia cutis resembling herpes zoster, I think that a better diagnosis than the one Dr. Zwick offered would be that of leukemia lymphadenosis of a zosteriform type.

Lichen Planus Hypertrophicus. Presented by Dr. Cole and Dr. Driver, Cleveland.

H. K. K., a white man, aged 46, whose family history was unimportant and who had not had tuberculosis, was first seen in 1925, complaining of an eruption on the legs of five years' duration. Physical examination at the time showed a typical erythema induratum over both shins. We advised the patient to have his tonsils removed, and the local process was treated by roentgen therapy, with a

moderate response. Later he was given treatment with quartz lamp irradiation, and this was followed by injections of sulpharsphenamine. Finally, in 1927, he was referred to a specialist in Cleveland because of the possibility of tuberculosis. The specialist was unable to find the focus. A course of injections of tuberculin was advised, which was given. This was later followed by a course of injections of gold and sodium thiosulphate, which lasted for about a year. The patient returned to us again in September, 1931, complaining of pruritic lesions over the abdomen and genitalia and in the axillae.

Distributed over the lower part of the abdomen, especially on the right side, were raised, sharply defined, brownish nodules, varying in size from that of a pea to that of a cherry, with a papillomatous appearance, and a great deal of induration. Smaller similar lesions were present in the left axillary space and under the scrotum, while over the dorsum of the glans penis were numerous, rather shiny, violaceous, slightly raised, papular, sharply defined lesions. The patient still shows some ill-defined, slightly reddish, somewhat subcutaneous nodules over the shins, especially on the left leg. There are some violaceous papules in a retiform arrangement on the inside of the cheeks, especially the left cheek.

Histologic examination of a verrucous lesion taken from the abdomen showed an extensive hyperkeratosis and parakeratosis of the epidermis with a cellular infiltration in the upper part of the subcutis, especially involving the papillae. This cellular infiltrate was sharply defined in a bandlike form against the rest of the cutis. There was a certain amount of infiltration around the blood vessels.

The impression obtained is that the condition is lichen planus hypertrophicus, probably after treatment with a heavy metal preparation, of the type that has been described following treatment with arsphenamines, as well as after injections of gold compounds.

A Case for Diagnosis (Atrophic Lichen Planus-Lymphoblastoma?). Presented by Dr. Cole and Dr. Driver, Cleveland.

V. C., a white man, aged 40, a laborer, was first seen in March, 1926, complaining of a severe generalized pruritus of five years' duration. He had been employed by an oil company, cleaning out pipe lines through which oil and gasoline had passed. Examination at this time showed a generalized, scaly, erythrodermia over the entire body. There was a rather marked, generalized adenopathy. At this time we believed that the condition belonged in the group of lymphoblastomas, although there was a possibility that it was merely a generalized dermatitis exfoliativa, secondary to a dermatitis venenata. In January, 1927, following a visit to Italy where he had been treated with sulphur baths without improvement, the patient again presented himself. At this time he was placed in Lakeside Hospital for observation and study. Studies of the blood and biopsy did not reveal lymphoblastoma. Treatment consisted in the application of ointment of boric acid, U. S. P., and roentgen rays. The skin over the entire body became markedly thickened and pigmented. About this time a marmoraceous mottling consisting of erythematous areas set off with a vascular reticula developed on the arms and neck. On the right arm there was a dollar-sized area of atrophy with telangiectasia. The general thickened condition of the skin gradually subsided, but the atrophic areas on the neck and arm remained, and in September, 1929, the condition resembled atrophic lichen planus. Under roentgen treatment this condition practically disappeared. The patient had not received much roentgen treatment.

In May, 1931, the patient reappeared, after having remained well for nearly two years. He now complainted of generalized pruritus, which was particularly marked on the flexor surfaces. He stated that he was unable to work, that the condition became aggravated when he became overheated and that he had difficulty in sleeping. Examination revealed an eruption in each supraclavicular space, particularly on the right, made up of a marmoraceous, deep, red network, with whitish skin between the meshes of the reddish lesions. Definite evidence of atrophy was present. Three small scars from biopsies were seen. There was a

slight extension of the process on the back of the neck and an area of thickening over the nape of the neck. There was also one area of alopecia of the scalp. There was a portion under the arm about the size of a silver dollar, showing similar atrophic changes and scar formation. There was no involvement of the mouth. There was dystrophy of the nails of both thumbs and the third finger of the left hand. There was evidence of redness and atrophy of the skin on both elbows, and also diffuse redness and scaliness over both shins. There was marked pityriasis of the scalp. Examination of the blood gave negative results.

Biopsy performed on a section of the epidermis showed marked thinning and lack of papillae. The upper corium showed a slight, but diffuse infiltration of round cells and isolated areas of marked infiltration. The vessels were increased in number and were dilated, showing a perivascular infiltration of round cells. Pigment cells were scattered through the upper part of the corium.

ANNULAR LICHEN PLANUS. Presented by DR. H. G. MISKJIAN.

E. Y., a colored woman, aged 30, from the service of Dr. Cole and Dr. Driver at Lakeside Hospital, was first seen in the dermatologic dispensary on account of a follicular syphiloderm. After the fourth injection of arsphenamine she complained of malaise, sore throat and swelling in the neck. Markedly enlarged tonsils, swelling of the parotid glands and edema of the eyelids were found. Arsphenamine was discontinued temporarily and bismuth salicylate given. After one month the condition subsided, and arsphenamine therapy was reinstituted in conjunction with bismuth. The family history was irrelevant.

The general physical examination gave normal results. Distributed over the skin of the entire body there were many lesions, varying in size from 1 to 3 cm. The individual lesions were annular, thickened and infiltrated, with atrophic and darkened centers. At the sites of trauma (needle punctures), there were flat angular papules.

Laboratory examination of the blood showed a Wassermann reaction of 4 plus; the blood count showed red cells, 4,410,000, 9,600 white cells and a normal differential count. The urine was normal. Examination of the spinal fluid gave entirely negatives results. Histologic examination of a section of the specimen showed a small fragment of tissue which was covered with a hypertrophic layer of stratified squamous epithelium. The surface was flat and was covered with keratinized material. The basal layers were sharply delimited, but the rete malpighii varied in length. Immediately beneath the basal layer there was an infiltration of mononuclear round cells.

DISCUSSION ON PAPERS OF DRS. COLE AND DRIVER AND DR. MISKJIAN

DR. E. D. OSBORNE, Buffalo: I thought that the case presented for diagnosis was exceedingly interesting. I spent considerable time going over the history in an effort to come to a definite diagnosis and am willing to agree to the possibility that the lesions that involve the palms are due to lichen planus. I remember two or three patients who had lesions on the palms and soles resembling those in this case very much. I should like to have the question of the possibility of an arsenical poisoning ruled out definitely. On the other hand, the lesions on the hands and the dystrophy of the nails resemble those of a case on which Dr. Cole has written and which many of us have seen. I think that the histologic observations are typical of lichen planus.

DR. KARL G. ZWICK, Cincinnati: Referring to the case presented for diagnosis, while there is a possibility that arsenic is a factor in the case, I must point out the white plaque with a distinct, fine network on the buccal mucous membrane. I do not think that such whitish striated plaques are ordinarily associated with arsenical keratosis; they are seen in lichen planus.

DR. H. N. COLE, Cleveland: Of course, I have seen this patient and followed him many years. A dermatitis due to oil first developed and the condition of the nails followed the exfoliating dermatitis. So far as the neck is concerned, this

process does not show the regular arrangement of the papules seen in dyskeratosis congenita. There is not the brownish-red papule with the white surrounding base. It is true that the local condition on the neck is somewhat like that in the other patient. This would not come to mind if he did not have the condition of the nails also. So far as the histologic picture is concerned, the condition is a lichen planus, and he has at present a lichen planus in the mouth on the inside of the cheeks.

EPITHELIOMA ADENOIDES CYSTICUM (OF BROOKE). Presented by DR. J. V. AMBLER.

J. M., a white man, aged 37, from the service of Dr. Cole and Dr. Driver at Lakeside Hospital, stated that the onset of the condition occurred twenty-two years prior to presentation, when he first noticed the formation of many nodular growths about the eyes and nose. In the course of a year the nodules increased in size and spread in the extent seen at the time; the lesions have not increased but have remained stationary and have been symptomless. No therapy has been attempted. The family history was irrelevant. Examination shows a conglomeration of sessile and semipolypoid, yellowish-white, pearly nodules, varying in size up to 1 cm. in diameter, situated between the eyes and over and around the nose. Pores and comedones, from which a whitish sebaceous material can be squeezed, are conspicuous. Similar, but smaller, nodules are thickly scattered over the forehead, about the mouth, behind the ears, on the lower part of the neck and clavicular region, the upper part of the back, the back of the neck, and particularly between the scapulae. Medial to the angle of the left scapula is a freely movable, subcutaneous nodule about 1.5 cm. in diameter. There is also a similar subcutaneous nodule on the right side of the forehead at the hair line; otherwise, the patient is essentially normal.

Examination of the blood showed 5,800 white cells and 5,800,000 red cells; the differential count revealed: polymorphonuclears, 83 per cent, lymphocytes, 13 per cent, mononuclears, 3 per cent, and basophils, 1 per cent. The urine was normal. The Wassermann reaction of the blood was negative.

Biopsy revealed collections of tumor epithelial cells having a basal cell character, located in the corium and at no point connected with the surface epithelium. These masses of cells varied in size and configuration, and often showed short processes extending into the stroma. The individual cell of the tumors was small and had a narrow border of cystoplasm surrounding a nucleus, which was round, oval or spindle-shaped, and which stained more deeply than the central cells. Many of the masses contained cystic spaces in which there was acidophilic, homogeneous material and which were lined with several layers of parakeratotic cells. There was an increase in the connective tissue stroma which tended to be arranged in concentric layers about the tumor masses. Portions of it had the appearance of myxomatous degeneration, taking a pale stain. There was a slight infiltration of lymphocytes. The vascularity was not remarkable. The surface epithelium was thin; the granular and horny layers were prominent. The rete cones were in large part absent or were small and short.

SYRINGOCYSTADENOMA. Presented by DR. R. E. BARNEY, Cleveland.

S. L., a white girl, aged 19, entered the dispensary complaining of an eruption involving the eyelids and the upper part of the chest. There were no associated symptoms. The mother had similar lesions on the eyelids. The lesions have been present on the eyelids for as long as the patient can remember, but the chest became involved only three years ago.

The patient is a well nourished young woman who presents an eruption involving the upper part of the chest and the eyelids. The process is made up of pink, slightly elevated, firm nodules ranging in size from that of a glass pinhead to that of a small pea. Biopsy on a specimen taken just below the right axilla revealed changes typical of syringocystadenoma.

DISCUSSION ON THE PAPERS OF DRS. AMBLER AND BARNEY

Dr. Udo J. Wile, Ann Arbor: I think that in the case shown by Dr. Ambler from the service of Dr. Cole and Dr. Driver, that of the patient with the lesions on the face, the condition could readily have been mistaken for von Recklinghausen's disease, and unless I had seen the biopsy I should have questioned the diagnosis of epithelioma adenoides cysticum. Not only does the patient have tumors of a much larger size than those ordinarily seen, but he has a pigmentation on the body. The two cases illustrate admirably the difference between epithelioma adenoides cysticum and syringocystadenoma, which can be seen under the microscope. In Dr. Cole and Dr. Driver's case of Brooke's disease, the cystic changes were marked. The other case showed definitely the picture of benign cystic epithelioma. I think that these two cases are excellent examples of how different the conditions really are.

Dr. Karl G. Zwick, Cincinnati: As Dr. Cole and Dr. Driver's case shows a characteristic, though isolated, fibroma molluscum pendulum and several café-au-lait spots on the body, I should favor the diagnosis of a "case fruste" of von Recklinghausen's disease in addition to the pathologic condition described.

Dr. H. T. Phillips, Wheeling, W. Va.: In connection with the case of Drs. Cole and Driver, I am interested in the future therapy, as radium has been tried without much success. In the few cases I have treated, my experience is that destruction by cautery or electrodesiccation is the procedure giving the best results.

Dr. S. W. Becker, Chicago: I should like to subscribe to Dr. Wile's differentiation of these two conditions. The patient, aged 37, with epithelioma adenoides cysticum presented benign epidermal growth as found by Dr. Maud Slye of the University of Chicago in some of her mice with cancer. The clinical and histologic picture differs from that in the case of Dr. Barney.

Erythema Palmare Hereditarium. Presented by Dr. J. V. Ambler.

R. B., an Austrian Jew, aged 63, from the service of Drs. Cole and Driver at Lakeside Hospital, states that he first noticed redness of the palms seven years prior to presentation. This condition has remained stationary since the onset. There have been no subjective symptoms. The general health has been excellent, except for occasional attacks of abdominal pain. He was recently discharged from Lakeside Hospital where the diagnosis of chronic cholecystitis was made. The patient is a very heavy smoker, smoking a pipe; he has smoked almost constantly for fifteen or twenty years; he drinks from four to fifteen cups of coffee each day. There is no history of a similar condition in the parents or other members of his family.

Physical examination revealed a well nourished, well preserved man. There was a symmetrical redness of the palms which extended over the dorsum and the tip of all the digits up to the proximal end of the first phalanx. In the center of each palm was a triangular area in which the color of the skin was normal. The nails were slightly cyanotic and somewhat atrophied. There was a similar condition, to less extent, on both great toes. The erythema disappeared momentarily on pressure. The radial and dorsalis pedis pulsations were normal. The blood pressure was 120 systolic and 70 diastolic. Examination of the blood showed 9,250 white cells, 5,200,000 red cells, and a normal differential count. The urine was normal. The Wassermann reaction of the blood was negative. Chemical examination of the blood showed 23.5 mg. of urea nitrogen and 1.9 mg. of creatinine per hundred cubic centimeters.

The temperatures of the surface of the body are normal as compared with the control group of normal persons of the same age. The temperature readings of the palms, of the phalanges and of the dorsal surface of the phalanges are from 4 to 5 degrees centigrade higher than temperatures of these areas in the control group. (Readings of temperature were made with the Scott-Tycos dermatherm.)

DISCUSSION

DR. HENRY C. SHAW, Cleveland: When the patient was admitted to the service we thought that the case was of the type noted by Lane and reported in the ARCH. DERMAT. & SYPH. (**20**:445 [Oct.] 1929) which was also called "red palms."

DR. S. W. BECKER, Chicago: This patient presented hyperemia in the region of the nail folds. Leukonychia totalis of the nails was also present, though it was not mentioned in the history. We have recently studied in our clinic the case of a young woman with passive hyperemia of the fingers, which was confirmed by capillary studies of the nail folds, who presented leukonychia totalis of some of the nails. I should like to know what the capillary picture is in the nail folds of the patient presented.

DR. HENRY C. SHAW, Cleveland: That was merely a preliminary study. Capillary studies are to be performed. Local studies of the temperatures of the hands and skin revealed an increase of 5 C.

POROKERATOSIS (MIBELLI). Presented by DR. J. V. AMBLER.

W. D., a colored man, aged 35, from the service of Drs. Cole and Driver at Lakeside Hospital, states that he first noticed the disorder at 9 years of age, as a small keratotic lesion on the right thigh. He now complains of several keratotic lesions on the hands, scrotum, thigh, arm and scalp. The lesions on the hands are of about two years' duration. There has been no treatment except that an attempt to remove the large lesion on the left hand by some type of cauterizing agent was made about one year before presentation. The lesions have been symptomless except for slight itching. The family history as to diseases of the skin was irrelevant. The patient had the usual childhood diseases, gonorrhea twice and a chancre in 1913. In 1928 he received antisyphilitic treatment consisting of eighteen intravenous injections and a few injections given into the hip. Physical examination showed on each hand, scrotum, right thigh, right arm and scalp keratotic lesions, all of which had similar characteristics; the borders of the lesions consisted of an elevated, wavy, horny ridge, on the summit of which was a wavy line which encircled the lesion. With a scapel it could be demonstrated that the wavy line was made up of horny material set into a sulcus at the summit of the elevation. The lesions varied in size from that of a pea to that of a silver dollar. The largest lesion, that on the dorsum of the left hand, was roughly about 1½ inches (4 cm.) in diameter; the area within this encircling line was apparently almost normal. The lesion at the base of the right thumb was about 1 cm. in diameter, the central area being studded with curious stippled punctate depressions. General physical examination gave normal results, except for a soft systolic murmur heard over the aortic area. The urine contained many white blood cells, otherwise it was normal. The Wassermann reaction of the blood was 4 plus. Examination of the spinal fluid gave negative results. Histologic examination of sections showed an excessive amount of keratinization in which the horn cells were imperfectly cornified with preservation of some of their nuclei, and in which intermediate stages of cornification were not distinctly seen. No sweat glands or sebaceous glands were seen in the sections. While the histologic appearance is not inconsistent with porokeratosis, the sections do not show the essential features.

DISCUSSION

DR. UDO J. WILE, Ann Arbor: I think that this case is a splendid example of the disease, the first case I have ever seen in a colored person. The lesions occupy unusual sites, on the shoulders and on the trunk. Most of these lesions have been seen on the feet and on the hands. I wonder whether Dr. Cole has made a survey of the disease. I believe that few have been seen in the colored people.

Dr. H. N. Cole, Cleveland: I have not looked up the literature. This is the first case I have ever seen in a colored person.

Dr. E. B. Tauber, Cincinnati: We have had one such case in a colored person.

Pustular Psoriasis Associated with Dermatitis Repens. Presented by Dr. J. V. Ambler.

W. R., white, a physician, aged 29, from the service of Dr. Cole and Dr. Driver at Lakeside Hospital, dated the onset of his present illness to an infection of the left little finger following an injury in 1918. For three years following this injury, the little finger was a "mass of proud flesh," resisting all types of treatment. In 1922, he first noticed psoriasiform lesions on the elbows and the extensor surfaces of the thighs. The condition had persisted since then with frequent exacerbations. All of the attacks had been similar, consisting of generalized psoriasiform lesions accompanied by pustular formation and changes in the finger-nails. At no time since 1928 had the finger-nails been entirely free from lesions. He was admitted to Lakeside Hospital, on Feb. 12, 1931, at which time he had a generalized exfoliative dermatitis which covered the entire body with the exception of the face. The legs, feet, arms and hands were bright red and partially covered with large white scales. On close examination numerous small, pinhead-sized interdermal pustules were noted thickly scattered over the red areas. These pustules were especially evident over the fingers and toes. There was a symmetrical involvement of the finger-nails, the thumb, the fourth and fifth fingers of each hand being involved with deformed, markedly thickened, soft, piled-up nails and were very tender. The toe-nails showed an involvement similar to that of the fingers, but to a lesser degree.

Cultures from pustules and nails yielded Staphylococcus epidermides. The urine, the blood and the basal metabolic rate were always normal. The Wassermann reaction of the blood was negative. Biopsies showed subacute and chronic dermatitis. The patient was presented before the Cleveland Dermatological Society on Feb. 24, 1931. The consensus was that the patient was suffering from dermatitis repens with complicating pustular psoriasis. He improved slowly under treatment with various applications, protein shock with typhoid vaccine, ultraviolet light and autogenous vaccine. He was discharged markedly improved after three months' hospitalization and has continued to improve at home.

Pustular Psoriasis. Presented by Dr. Henry De Wolf.

F. G., a white man, aged 40, from the service of Dr. Cole and Dr. Driver at Cleveland City Hospital, had a cutaneous disease which began about five years before presentation as a scaly eruption of the scalp which soon involved the trunk and the extremities, especially the hands and feet. The nails of both hands and feet were always the most severely involved. He was treated with an ointment in the outpatient department, and did fairly well until the spring of 1931, when the disease became so severe that he could not walk. The eruption changed from a dry, scaly disease to a condition showing exudation, tenacious crusts and pustules. He was admitted to the hospital May 4, 1931, and in spite of various types of treatment he still has extensive lesions of the hands, feet and legs. The general health is unaffected.

Physical examination showed extensive lesions of the feet, legs and hands. The trunk was relatively free from lesions. The nails were greatly thickened, distorted and covered with a friable material. The involved regions were dusky red and covered with crusts and scales, and here and there small pustular lesions were present. There was an intertriginous dermatitis of the genitocrural regions. The Wassermann test of the blood was negative. Chemical examination of the blood showed a normal amount of sugar and urea. The urine was normal. A blood count showed: 4,100,000 red cells, 11,000 white cells and 80 per cent hemoglobin. The differential count revealed: polymorphonuclears, 70 per cent; small mononuclears, 24 per cent; large mononuclears, 5 per cent, and basophils, 1 per cent.

Biopsy showed that sections were covered by stratified squamous epithelium which in parts was thickened and formed elongated papillae that reached into the corium. In these regions the cornified epidermis was piled on top and infiltrated with polymorphonuclears. The interpapillary tissue and upper portion of the corium were loose, edematous and infiltrated by cells, mostly plasma cells, lymphocytes, and endothelial cells. This infiltration involved only the superficial layers of the corium.

DISCUSSION ON PAPERS OF DRS. AMBLER AND DE WOLF

DR. E. D. OSBORNE, Buffalo: I am willing to agree with the diagnosis in the first case, but the second case suggests blennorrhagic keratoderma in certain stages of development. The patient had gonorrhea fifteen years before presentation, but otherwise no symptoms had appeared since then. Another possibility is that of moniliasis such as that seen in the patient I presented at the 1930 meeting of the American Dermatological Association in Cleveland (ARCH. DERMAT. & SYPH. **23**:162 [Jan.] 1931), which strongly suggested the diagnosis of a psoriasis. We had three patients in the Buffalo City Hospital in whom the condition bore a close resemblance to that of the patient presented. They had keratoderma blennorrhagia.

DR. F. M. JACOB, Pittsburgh: The first patient has often been seen by the Pittsburgh society. Dr. Guy and I saw him about ten years ago. He had a patch of the nature of a dermatitis repens. The only treatment that affected the condition at that time was a 15 per cent solution of ammoniated mercury. Later, huge patches covering half of the thighs and back appeared. From a distance they resembled psoriasis, but on closer examination they showed oozing, crusting and scaling. The patient was brought to several meetings of the Pittsburgh society. Various types of treatment were tried, without success. Shortly before the patient went to medical school he was given an ointment of echinacia and citrine by an eclectic physician. The condition cleared up so quickly that I considered the remedy specific. I can now see that the patient is not well. The condition has recurred and has turned out to be pustular psoriasis.

DR. LESTER HOLLANDER, Pittsburgh: Pustular psoriasis and dermatitis repens caused me considerable chagrin at the Philadelphia meeting, as I reported citrine ointment to be a specific on the strength of this case which I also saw at Pittsburgh. Dr. Cole then arose and explained that the same patient was under his care and that further involvement had occurred.

DR. R. C. JAMIESON, Detroit: I had the same impression as Dr. Osborne on the second case, especially regarding the involvement of the joints. The case brought to mind a case of psoriasis in which I had unusually good results with intravenous injections of metaphen. The patient had previously tried everything, with no success, and after the use of metaphen intravenously for six weeks the condition was entirely cleared up.

DR. H. N. COLE, Cleveland: I might say we considered the possibility of keratodermia blennorrhagia. At present it resembles somewhat the keratoderma blennorrhagia. Urethral smears and smears from local pustules have all been negative. Moreover, the patient does not have gonorrhea. The picture has changed considerably in the last two or three weeks. At times there has been characteristic psoriasis with stippling of the nails, as well as other changes. I think that the condition is a true pustular psoriasis such as has been recently reported by Barber and others.

DYSKERATOSIS CONGENITA WITH PIGMENTATION (DYSTROPHIA UNGUIS AND LEUKOKERATOSIS ORIS). Presented by DR. H. N. COLE and DR. JOHN A. TOOMEY.

S. G., a white man, aged 22, had no familial history of a similar condition and had had the ordinary diseases of childhood. As far back as he can remember, he has had a peculiar condition of the finger-nails and toe-nails. Likewise, he

has had a peculiar, mottled type of pigmentation over the neck. He did not know that the skin over his tongue was different from that of other people. He said that his feet perspire freely and that he notices a great deal of perspiration on his hands. He said that occasionally large blisters appear on the heels of his feet and often remain for several weeks. These blisters are sometimes the size of a castor bean or even the size of a half dollar. Examination of the mucous membrane showed that the entire dorsum of the anterior two thirds of the tongue has a peculiar glazed, whitish appearance. The surface is rather smooth. The natural rugosities of the tongue do not show up well. The surface is likewise rather shiny, and here and there, distributed over the area, one will note small, bright red spots where there is a break in this leukoplakia-like formation. Over the entire palate there is likewise this glazed, whitish appearance. Over an area extending upward almost to the jaw, backward to just posterior to the ear, and downward in a straight line almost to the clavicles on each side and then converging from each side symmetrically to a point on the sternum about midway between the mammae, there is an eruption; it is most profuse over the anterior portion of the neck, down to the level of the clavicle, but involves all the areas described. It is of a peculiar, light reddish brown, or possibly grayish-red tint. It is made up of fine pinhead-sized, smooth, somewhat whitish papules, raised in linear rows, according to the somites of the skin, with a fine reddish base between the rows. Toward the outer border of the areas, the papules become less evident. Along the under surface of the upper part of the arm, extending from the axillary space, almost to the elbow, there are scattered discrete, macular brownish areas the size of, and smaller than, a pinhead. There is no evidence, however, of a papular formation. Over the knees there are numerous, slightly reddened, raised, follicular papules. The palms and soles show hyperhidrosis. There is a suggestion of thickening of the skin of the palms. There is no thickening of the soles. A definite crinkling of the skin and anetodermia are seen over the dorsum of each finger. There is extensive, universal dystrophy of all of the finger-nails and some of the toe-nails. Several of the toe-nails show pachyonychia. A section from the nails shows a low epidermis with parakeratosis and dyskeratosis. There were clumps of mononuclear elements and noniron-bearing pigment cells in the upper part of the corium, especially around the vessels. This case was described in full in the ARCHIVES (**21**:71 [Jan.] 1930).

LYMPHOGRANULOMATOSIS INGUINALIS. Presented by DR. HENRY DE WOLF.

J. F., a white man, aged 45, from the service of Dr. Cole and Dr. Driver at Cleveland City Hospital, one month before admission on Oct. 8, 1931, noticed a hard, painless swelling in the left groin. This swelling increased steadily until it became the size of a fist and tender to the touch. The patient gave a history of unprotected exposures just prior to the onset of the swelling, but stated that he did not have a penile sore or urethral discharge. He had had gonorrhea about eight years prior to admission to the hospital. He stated that he had not had lesions on the penis. Since admission to the hospital the course of the inflammatory process in the left groin has been indolent. Certain areas have fluctuated, and have been incised for drainage. Recently, the patient has received three treatments with filtered x-rays, without appreciable change.

Physical examination gave essentially negative results, except for the condition in the left groin where there was a large, relatively painless, deeply indurated, inflammatory process involving the inguinal lymph glands. Several small sinuses were found from which a seropurulent material was discharged. No penile lesions or scars of lesions were present.

The Wassermann test of the blood was repeatedly negative. Blood count showed: 4,900,000 red cells, 10,400 white cells and 90 per cent hemoglobin. The differential count revealed: polymorphonuclears, 52 per cent; small mononuclears, 42 per cent, and large mononuclears, 6 per cent. Smears and cultures of aspirated pus gave negative results for all organisms. Intradermal tests with the Frei

type of antigen have given repeatedly positive results. Interdermal tests with chancroidal antigen have given negative results.

LYMPHOGRANULOMATOSIS INGUINALIS. Presented by DR. HENRY DE WOLF.

S. W., a white man, aged 27, from the service of Dr. Cole and Dr. Driver at Cleveland City Hospital, has had swollen, painless glands in the left groin for the past six weeks. He said that he had had exposures prior to the onset of the complaint, but that he had not had a penile lesion or discharge. He was admitted to the hospital on Nov. 7, 1931. In spite of rest in bed and intravenous injections of typhoid vaccine, the adenitis persists and has increased slightly in size. The patient had gonorrhea in 1925, but said that he has not had a penile sore. In 1931 he had pleurisy of the left side of chest following influenza. Examination revealed a mass of four or five glands in the left groin which were enlarged to the size of small eggs, and were firm and painless to palpation. No evidence of a penile lesion was found. General examination revealed nothing important.

The Wassermann and Kline tests of the blood were negative on seven examinations. The intradermal test with the Frei type of antigen was positive. Such a reaction is present on the forearm. Puncture of the glands gave negative results for Spirochaeta pallida. A roentgenogram of the chest showed chronic pleurisy of the left side. There were 4,610,000 red cells, 10,300 white cells and 90 per cent hemoglobin; the differential count showed: polymorphonuclears, 67 per cent; small mononuclears, 26 per cent; large mononuclears, 4 per cent, and transitionals, 3 per cent. The urine was normal.

LYMPHOGRANULOMATOSIS INGUINALIS. Presented by DR. HENRY DE WOLF.

In R. S., a colored man, aged 31, from the service of Dr. Cole and Dr. Driver at Cleveland City Hospital, penile lesions developed three and a half months before presentation following numerous exposures. Two weeks following the appearance of the penile lesions the glands in both groins began to enlarge. The patient went to Charity Hospital Dispensary, where he was treated for syphilis, six intravenous injections having been given. He also received four intramuscular injections. The Wassermann reaction of the blood was 4 plus. The penile lesions healed, but the swellings in the groin continued to enlarge. In addition to the aforementioned complaints he has recently had scabies, for which he has been treated. In 1921, he had a penile lesion which was complicated by a bubo in the left groin.

Physical examination showed a well developed and well nourished Negro. The skin showed a healing scabetic eruption. On the penis there was a healed lesion on the coronary sulcus. Scars of the bubo which developed in 1921 were present in the left groin. There was enlargement of the inguinal lymph glands on both sides. The glands were indurated and matted together. In some areas there was superficial fluctuation. Small, draining sinuses were present on both sides. The discharge from these sinuses was seropurulent.

The Wassermann tests of the blood and spinal fluid were negative. An intradermal test with the Frei type of antigen gave a strongly positive reaction for lymphogranulomatosis inguinalis. A reaction is apparent at present. Examination of the blood showed that there were 4,000,000 red cells, 10,800 white cells and 70 per cent hemoglobin; the differential count revealed: polymorphonuclears, 60 per cent; small mononuclears, 23 per cent; large mononuclears, 16 per cent, and transitionals, 3 per cent.

DISCUSSION ON PAPERS OF DR. DE WOLF

DR. HENRY DE WOLF, Cleveland: We thought that it would be interesting to show these three patients with positive cutaneous reactions on the forearms. We have seen an increasing number of cases of this type, and the question of differential diagnosis arises constantly. In one case, that of the younger white

man, the glands were suggestive of a syphilitic adenitis. In this case there was no history of a syphilitic lesion or of a lesion on the penis. We have watched this man for five weeks. The Wassermann test has been negative repeatedly. The Frei test gave strongly positive results. The histologic picture of the glands shows the multiple areas of necrosis typical of the disease described by Nicolas and Favre in 1913.

Dr. Marion B. Sulzberger, New York: We have seen several such cases in New York. The subject is much too long to be discussed in detail here. I am interested to find that such cases have appeared in Cleveland. I do not know about the other parts of the United States. The first evidence of infection is often overlooked. It is usually an extremely small penile lesion following exposure. Later there is a glandular reaction, which is chronic and suppurative. It is now generally accepted that the condition is a venereal disease and follows intercourse. I concluded that in New York it was probably brought in by foreigners or by sailors coming in from foreign parts, as it is found mainly in sailors and longshoremen and their associates. It is possible that it has found its way to the cities on the Great Lakes because salt and fresh water sailors often associate with the same women.

The Frei test is considered to be specific. We have had a few examples in New York, and a positive reaction was also obtained with two antigens I obtained from Europe. This identifies the cases seen here with those reported in Europe. The question of therapy is much more difficult.

Dr. H. N. Cole, Cleveland: Dr. Miskjian who was working in our clinic first noted these peculiar types of glandular reactions which were different from chancroidal buboes and syphilitic glands. He designated them hypertrophic buboes, and felt that they constituted an entirely different disease. Then we began to read about the work of Nicolas and Favre and the work of Frei and of his success with an antigen test for this condition. Drs. Van Cleve and De Wolf have been working with this antigen, prepared in our own clinic, for the past two years. We have found that the test gives a positive reaction in lymphogranuloma inguinalis and in no other condition. We use the test a great deal in differentiating between chancroids, granuloma inguinalis and syphilis. We are convinced that the disease described by Nicolas and Favre is a distinct entity.

Dr. H. J. Miskjian, Cleveland: In 1924, while working on the treatment for chancroidal buboes, I became conscious that there were certain types of buboes that were quite different. Moreover, they did not respond to the injection therapy that we gave for the treatment of ordinary chancroidal buboes. We termed these cases hypertrophic buboes. We now feel that they are examples of the condition described by Nicolas and Favre, though there is a question in my mind whether hypertrophic buboes with periglandular necrosis is exactly the same condition as lymphogranuloma inguinalis.

Dr. E. D. Osborne, Buffalo: I cannot let this opportunity go by without saying that in our service in the Buffalo City Hospital we are always on the lookout for such cases, and we have not had any. Either the colored people are purer in Buffalo than in Cleveland, or perhaps the salt water sailors transfer it to the fresh water sailors at Cleveland only.

Dr. Lester Hollander, Pittsburgh: We have a number of these cases in Pittsburgh among our colored population.

Multiple Telangiectasia in Skin and Subcutaneous Tissue and Severe Secondary Anemia. Presented by invitation by Dr. Norman C. Wetzel.

N. S., a white boy, aged 9, from the Babies and Children's Hospital, Cleveland, was admitted to the Babies and Children's Hospital on Nov. 12, 1931. At birth an egg-sized mass was noted over the precordium, and several pea-sized growths were noted on both feet. Similar growths of varying sizes have appeared from time to time on the body, and at present eighty-eight can be counted. The patient

was often in a hospital for several years, the diagnosis of multiple hemangioma being made. Many treatments have been instituted—surgical removal and removal with boiling water and treatment with radium and with ultraviolet rays. The boiling water method proved the most successful. At first the growths would be small; later they would grow larger, and a few would then disappear spontaneously. General development was normal until three years before admission to the hospital, but since then the patient has grown progressively weaker and more pale. Occasionally he has become faint. There is no external bleeding, but occasionally there is evidence of a small amount of blood in the stool. The patient has never had a good appetite; he dislikes vegetables and drinks a great deal of milk. He has regularly taken pills of ferrous carbonate, U. S. P., for the past few years. The familial history was irrelevant.

Physical examination showed a poorly developed and nourished boy with a greenish-yellow pallor. He was not acutely ill, and quite alert mentally. There were about eighty-eight growths over the body, some of which were subcutaneous and some intracutaneous. The superficial ones were bluish, and the deep ones did not show through the skin. They were round, varying in size from that of a pea to that of a lemon and were rather soft. The eyegrounds showed marked papilledema, the edges of the disks were hidden; the cups were obliterated, the disks were pale in the deep layers. The vessels were engorged and tortuous throughout. There were no definite hemorrhages or exudates. A small patch of minute, tortuous vessels in a small area of the retina in the upper temporal periphery of the right eye was suggestive of an early angiomatous formation. The heart was slightly enlarged, and a systolic murmur was heard over the whole precordium.

Examination of the blood on admission to the hospital showed: hemoglobin, 20 per cent; red cells, 2,700,000; white cells, 6,000; myelocytes, 1 per cent; polymorphonuclears, 65 per cent; small mononuclears, 28 per cent; large mononuclears, 2 per cent; eosinophils, 3 per cent; reticulocytes, 1.4 per cent. On Dec. 9, 1931, there were 55 per cent hemoglobin and 4,300,000 red cells. Bleeding and clotting times were normal. Treatment with 2 Gm. of saccharated ferrous carbonate administered twice daily was started on the twelfth day in the hospital. The regular diet was given.

Histologic examination by Dr. A. R. Moritz showed that the epidermis was thin, but that the stratum corneum was as thick as the remainder of the epithelium. The granular layer was prominent; the rete cones and the individual cells of the rete malpighii showed no alteration. The papillary layer was not altered. In the deep corium and subcutis there were a number of vascular spaces varying greatly in size and in outline. These spaces were lined by a single layer of endothelium, and some contained fibrin enmeshing erythrocytes. In general, the vascular spaces lay in a stroma made up of fibrous connective tissue, the nuclei of which were moderately abundant and spindle-shaped. In several focal areas the vascular endothelium lining the small vascular spaces was hyperplastic, and in several instances mitotic figures were recognized. Deposited in the stroma about these vascular spaces there were small deposits of brown granules of pigment. The sweat glands showed no alteration; hair follicles were not seen in this section.

Sections from a larger specimen showed many vascular spaces varying in size and outline, and often anastomosing with one another. Some of them were filled with fibrin and erythrocytes. In general, the supporting tissue was of the collagenous fibrous connective tissue type, but there were portions in which the vascular tissue extended into adipose tissue and striate muscle which were distributed on the fibro-adipose tissue. The diagnosis of telangiectasia in the skin and subcutaneous tissue, exhibiting thrombosis in various areas, was made.

DISCUSSION

DR. NORMAN C. WETZEL, Cleveland: While the vascular lesions are obviously of the greatest dermatologic concern, the severe anemia that has developed in this patient has attracted even greater attention from our own pediatric point of view.

But in commenting first on these vascular deformities, I should merely like to call attention to the fact that at biopsy the condition was first interpreted as multiple hemangiomas, but was later more correctly thought to be an instance of telangiectasia. Indeed, Dr. Moritz assures me that the histologic features greatly resembled those recently described again by Goldstein in discussing Rendu-Osler-Weber's disease, though it should be pointed out that the characteristic hemorrhages have not appeared in our patient. Nevertheless, it is clear to me that the correct terminology or diagnosis is purely a pathologic and dermatologic matter, to which we as pediatricians can contribute nothing. Dr. Cole was also tremendously interested in the anemia and has requested that I stress this feature in the discussion.

You will recall from the chart and résumé of the history that the patient had been receiving pills of ferrous carbonate regularly for the past few years without effect; that other measures had been tried to combat the anemia, and that in spite of all therapy the hemoglobin in the blood remained at a level of 20 per cent, and there were 2,500,000 red cells and a white cell count of 6,000. Meanwhile, however, the patient had received radium therapy, and anorexia had also developed to the point where the patient was subsisting on little else than milk. We believe that the key to this hematologic situation is to be found in the fact that the initial icteric index was 5 plus, that is to say, at the upper level of normality, in spite of an extremely low value for hemoglobin and a low red cell count. For it is distinctly unusual and indeed theoretically impossible that a pure nutritional anemia manifest a comparatively high icteric index, and we are therefore obliged to lay considerable stress on slight but definite destructive processes which are contributing not only to the anemia but also to the maintenance of such a level of pigmentation. Coupled with this, of course, is the coincident deficit in iron of an exclusive or almost exclusive diet of milk, and, parodoxically enough, a deficit in iron in spite of the administration of pills of ferrous carbonate, U. S. P., the therapeutic value of which was absolutely nil. On the other hand, the destruction of blood could easily be enhanced in this patient because of the obvious slowing of the blood stream through the tremendously dilated vascular channels; in support of this theory, it is interesting to note that Dr. Moritz has found massive deposits of pigment in the endothelial linings. Finally, there is every reason to believe that the nutritional factor, or more precisely the deficit in iron, contributed predominately to the development of the anemia in view of the fact that we were able to demonstrate a prompt and unquestionable response to the administration of iron, given twice a day in the form of 2 Gm. of saccharated ferrous carbonate, within a period of thirteen days.

Dr. Udo J. Wile, Ann Arbor: It is difficult for me to understand how this condition can be classified as telangiectasia. There are definite angiomata cavernosa. Twenty-five years ago when I was in a pathologic service, I assisted at a postmortem examination of a child who died following hemorrhages. As in this case, there were numerous lesions over the body, some of which were superficial, and many, deeper. In addition, there were numerous angiomata cavernosa in the liver, and it was from these that the child bled to death. I think that the question of anemia in relationship to the angiomatous tumors can be explained by the fact that the walls are extremely thin and physically subject to trauma. The escape of blood into the surrounding tissues may explain it. This child had also a large angioma at the base of the liver. I cannot see how this can be called a case of multiple telangiectasia rather than one of multiple angiomas.

Sarcoid (Boeck)? Presented by Dr. E. W. Netherton, Cleveland, Ohio.

In S. F., a white man, aged 47, a painter, a small brown nodule developed back of the right ear three years prior to presentation. It became enlarged and was removed surgically. There was a recurrence, and this growth was also removed. Seven months later a few nodules appeared on the back and on the

lateral surfaces of the left arm. A small nodule has since developed on the sternum and one on the right ala of the nose. There are no subjective or constitutional symptoms.

The patient was first seen in January, 1931, at which time there were several raised, flat or somewhat nodular, dark brownish-red tumors on the lateral surfaces of the left arm, on the back, over the sternum and on the right side of the nose. Smooth and numerous small telangiectases were present on the surface. They varied in size from that of a pea to that of a quarter of a dollar. Diascopic examination revealed areas of infiltration throughout the lesions. In back of the right ear there was a larger, more nodular lesion of the same nature, with the exception of some central scarring which had resulted from operative interference.

Roentgen rays, radium and carbon dioxide snow, as well as arsenic administered internally, failed to produce any change in the lesions; therefore, the patient had had a number of them removed surgically. However, at present the lesions may be seen on the back of the right ear and on the right ala of the nose, and there is a small lesion on the sternum. The lesion on the back of the ear is infiltrated, slightly nodular, varying in hue from brownish pink to yellow and granulomatous, with small telangiectases on the surface. Biopsy showed that the epidermis is practically normal. In the corium there was a diffuse, inflammatory infiltration which consisted of numerous, ill-defined areas which were separated by a small amount of collagenous fibrous tissue. A few areas were sharply defined. The infiltration consisted of proliferation of connective tissue, numerous, large endothelial cells, and also a large number of eosinophilic leukocytes and neutrophilic leukocytes. There were no tubercles or giant cells. Throughout the infiltration there was dilation of the blood vessels, and in some areas of the section perivascular infiltration was easily seen. There were no areas of hemorrhage or deposits of pigment. A section stained for tubercle bacilli revealed no organisms.

SARCOID (BOECK). Presented by DR. COLE AND DR. DRIVER, Cleveland.

Mrs. L. D., a white woman, aged 22, who had never been pregnant and had been married for two years and whose personal history was essentially negative, a little over one year ago noticed a lesion on the nose which reached the size of a cherry and was rather red. A month or so later a similar spot appeared on the left arm, and soon afterward one on the right arm. Since then fifteen or twenty smaller ones have appeared over the face and arms, and recently a few on the buttocks. The spots have never completely disappeared, and none of them has broken down. There are no local symptoms in connection with them; the patient has been nervous, has had periods of vomiting occasionally and has lost considerable weight. Some time prior to presentation she had an attack of urticaria which lasted for a week or so.

Physical examination showed a deep, bulbous, indurated, cherry-sized tumor at the end of the nose, and distributed over the forehead, cheeks, arms and buttocks were numerous light bluish-red cutaneous and subcutaneous tumors; they were painless, and varied in size from that of a pea to that of a castor bean. Examination of the heart and lungs showed nothing remarkable. The liver and spleen were not palpable. The urine was normal. In each axilla, under the jaw, and in the left groin there were hard, discrete glands ranging in size from that of a pea to that of a navy bean. The Wassermann reaction of the blood was negative. There was a diffuse form of swelling of the phalanx of the index finger of the left hand. It showed no tenderness, and a roentgenogram showed a certain amount of bone absorption.

The section examined at biopsy showed a low epidermis and richly cellular nests of epithelioid cells, with pale-staining nuclei throughout the entire corium, even deep down into the corium itself, and in connection with them small round cells were noted. These cell nests were separated by collagenous septums. There was no evidence of caseation.

The patient has been under observation and has received roentgen therapy and arsenicum, with little or no result. She was given injections of gold and sodium thiosulphate intravenously with benefit for a time, but a slight erythematous eruption developed over the abdomen, so this was discontinued. The patient also has received bismuth, with questionable results.

DISCUSSION ON PAPERS OF DR. NETHERTON AND DR. COLE AND DR DRIVER

DR. J. R. DRIVER, Cleveland: Both of these cases are more or less typical examples of Boeck's sarcoid. Our case is interesting from the standpoint of involvement of the bone of one finger. There is a definite absorption of bone.

DR. E. D. OSBORNE, Buffalo: I should like to know how many patients with Boeck's sarcoid have been cured by the use of gold compounds.

DR. H. C. COLE, Cleveland: We have tried it on our patient. It did not seem to benefit her very much. Possibly she improved for a time, but then a dermatitis developed and we discontinued its use. I am not familiar with the literature, but believe there have been some favorable reports.

DR. E. W. NETHERTON, Cleveland: The case I presented was not as typical histologically as that of Dr. Cole and Dr. Driver, and there may be some question as to the diagnosis. The lesion was removed surgically. There was a question of this condition being Hodgkin's disease.

A CASE FOR DIAGNOSIS. Presented by DR. COLE and DR. DRIVER, Cleveland.

Mrs. M. B., a white woman, aged 43, entered the Lakeside Hospital on Nov. 16, 1931, complaining of a sore on the left hand. The patient lives on a farm and is very active in taking part in the work on the farm. One month before admission she had helped her husband in taking care of a flock of sheep that had sore noses and mouths. During the past month on two or three occasions she had picked up the remains of dead rabbits that the cats had dragged in. There was no history of injury to the hand. Ten days before admission she noticed three small vesicles situated on a reddened base, on the left thumb. Two days before admission these lesions began to extend and rapidly coalesced, forming two large dark blue bullae. The hand became markedly swollen, and the whole forearm felt numb; there was no tenderness. The husband had had a similar but smaller lesion on the hand, which had involuted. On the dorsal aspect, at the base of the left thumb, there was a palm-sized, raised tumor with an indurated bright red base surmounted by two large deep bluish tense bullae about the size of pigeon eggs. On the flexor surface of the same forearm, a little above the wrist, there was a similar dime-sized vesicle with a surrounding area of erythema. Neither lesion was painful. On aspiration the contents of the lesion were found to be thick and gelatinous. There was a faint red streak up the medial surface of the arm. The axillary lymph glands were not enlarged. The patient had a low grade fever. Two or three days after admission, a small, raised, vesicular process developed on an erythematous base around one side of the nail of the second finger on the other hand. General physical examination revealed nothing abnormal. The blood picture was also normal. All bacteriologic tests and inoculations into animals gave negative results. Agglutination tests for tularemia gave a negative reaction. A patch test for phenolphthalein was negative. The Prausnitz-Küstner test for phenolphthalein gave a positive reaction.

Biopsy showed marked edema of the epidermis, especially of the upper portion of the corium. The section showed an enormous epidermal formation of bullae, and in one portion of the section the edema in the upper portion of the corium was so extensive that the entire area was almost a confluent bullous subepidermal lesion. The section showed intense cellular infiltration around the vessels, and in the upper portion of the corium this cellular infiltration was general. It was made up of mononuclears, with a liberal sprinkling of eosinophils. This cellular

infiltration around the vessels extended deep down into the corium, and there was a certain amount of it around the coil glands as well.

DISCUSSION

DR. KARL G. ZWICK, Cincinnati: The result obtained with a modification of the Prausnitz-Küstner technic deserves special attention and calls for further investigations with the modified procedure.

DR. MARION B. SULZBERGER, New York: I agree with Dr. Zwick. I have never seen a passive transfer of phenolphthalein sensitivity, nor has such a transfer been reported to my knowledge. Several authors have reported such a passive transfer of other definite chemicals, but in all cases the method, technic and conclusions have been subjected to much criticism. It is difficult to get phenolphthalein into an aqueous solution, and an alcohol solution may be responsible for the apparent reaction. Aside from that I think that this condition is clinically a type of eruption due to a drug, possibly phenolphthalein.

DR. HENRY C. SHAW, Cleveland: The patient's blood serum was inactivated by heating in the water bath at 56 C. for two hours. Two intradermal injections of this serum were made into the arm of a person who had not taken phenolphthalein. On the following day a sponge saturated with a 1 per cent alcoholic solution of phenolphthalein was applied at the site of one wheal and another normal area. On the following day, the site into which serum had been injected and to which the phenolphthalein had been applied presented an infiltration 1 cm. in diameter, which persisted for forty-eight hours. There was no reaction at the sites where the serum had been injected or phenolphthalein had been applied alone. I make no interpretation of this reaction.

DR. MARION B. SULZBERGER, New York: That would be an entirely new type of transfer.

PSEUDO-ACHROMIA POSTPARISITARIA—TINEA VERSICOLOR. Presented by DR. R. E. BARNEY, Cleveland.

J. M., a white girl, aged 16, first seen Oct. 17, 1930, stated that in June of this year she noticed brown, scaly, itching patches over the trunk. Three months after the appearance of these patches she took sun baths. Following this procedure the brown spots disappeared, leaving white areas.

Examination on October 17, showed a well nourished girl, who presented an extensive depigmentary process over the chest and back. The borders of these areas were convoluted, suggesting that the larger patches resulted from a confluence of smaller ones. Outside the larger depigmented areas were similar satellite lesions varying in size from that of a glass pinhead to that of a quarter. There was no associated scaling or inflammatory reaction. Repeated examination of scrapings of the skin did not reveal spores or hyphae. The patient was reexamined on Nov. 20, 1931, at which time she presented typical tinea versicolor involving the trunk. Scrapings of the scales digested in a 10 per cent solution of sodium hydroxide showed Microsporon furfur. In addition, the arms revealed numerous small pea-sized white macules.

DISCUSSION

DR. MARION B. SULZBERGER, New York: This case is interesting to me on account of the fact that about two months ago a well dressed, nice looking young woman came into the office of Dr. Wise, with whom I am associated, and asked for treatment of a rather generalized pigmentary disturbance. The problem was important on account of the décolleté. On examination I found tinea versicolor. There were scattered, lighter colored lesions on the trunk, almost identical with those in this case, and microscopic examination demonstrated the fungus in the scales at the edges. It is generally supposed that the lack of pigmentation following tinea versicolor is due to the protection of the brown fungi covering these areas, which thus do not become exposed to the pigment-producing rays.

The conclusion is that when tinea versicolor heals, the areas that have been protected are less pigmented. We know that we are able to produce pigmentation in normal skin within two or three weeks, or less, with ultraviolet treatment and oil of bergamot. If the lack of pigmentation in these cases were due to simple physical action of the shielding fungus layer, the pigmentation should reappear rapidly. I notice that Dr. Barney has produced little or no pigment since October 17, in spite of sunlight and treatment indicated for the formation of pigment. I had promised our patient that within from three to six weeks she would have a normally pigmented skin. In spite of regular treatments with ultraviolet light and bergamot oil, I could not demonstrate that pigment had returned in any of the depigmented areas. It seems to me that the cases of lack of pigmentation and pityriasis versicolor are not all alike, and that in some of them, such as this one, the fungus seems to have destroyed or paralyzed the pigment-forming cells. Whether this is due to poisoning of Bloch's oxidase or not, I cannot say, nor can I say for how long a period the cells lose their pigment-forming ability. But I believe that in Dr. Barney's case and in two cases I have observed, the lack of pigmentation does not seem due to the simple shading of an area of skin through the physical properties of the covering of fungus.

These cases differ somewhat in their clinical appearance from the usual lack of pigmentation so frequently seen in tinea versicolor, and they do not recover normal pigmentation in the manner one would at first expect. I think the cases well worth exact study, particularly in respect to the question of the destruction or paralysis of pigment formation.

Dr. R. E. Barney, Cleveland: When first observed this patient revealed an extensive, suggestively depigmentary process involving the trunk, as indicated in the photograph. Several weeks ago she again returned, and presented typical tinea versicolor involving, so far as could be determined, those areas which before were depigmented. In addition, numerous depigmented macules were seen on the arms. Kistiakowsky's explanation (*Ann. de dermat. et syph.* **1**:1264, 1930) for the depigmented areas is that ultraviolet rays are filtered out by the scale and the fungus. Following the disappearance of the scale and fungus, the depigmented areas remain.

Dr. Karl G. Zwick, Cincinnati: If I understand this case report correctly, the macular depigmentation is persistent, so that the designation achromia would seem to be more in accord with the actual condition than the term pseudo-achromia.

As I interpret it, the appellation, pseudo-achromia, applies to the absence of pigment revealed in the following case: A patient in whom I had found an infestation with Microsporon furfur, desired, last fall, to be relieved from it. After this had been accomplished, the skin presented a variegated appearance with brown and white areas. Examination and anamnesis revealed that the color in the brown areas was due to a persistent coat of tan, whereas in the pigment-free, white, i. e. pseudo-achromic areas, the fungus had protected the skin against the strong sunlight to which the patient had been exposed all summer while rowing on the Ohio River.

Precocious Tertiary or Malignant Syphilis. Presented by Dr. E. W. Netherton, Cleveland.

Mrs. H. T., a white woman, aged 33, first seen on March 11, 1931, had an indurated, superficial ulcer on the flexor surface of the distal phalanx of the right middle finger. The epitrochlear lymph node was enlarged. This had developed following injury with a comb, received while she was working in a beauty shop. Dark-field examination gave positive results. The Wassermann reaction was 4 plus, and the Kahn 4 plus. A few weeks prior to this examination her husband had secondary syphilis.

From March 11 to May 6, the patient received five injections of arsphenamine (2.2 Gm.) and two of neoarsphenamine (0.9 Gm.) and three injections of 1 cc. of a bismuth preparation. On May 6, several flat, shiny or slightly scaly, brownish-

pink, infiltrated papules the size of a pea and smaller appeared on the face and arms. These enlarged and new ones appeared. Squamous and corymbose lesions developed regardless of treatment. On July 1, a moist lesion developed on the right side of the nose; dark-field examination gave positive results. On July 21, she was given typhoid vaccine intravenously. Three elevations of temperature, one to 102 F. and two to 104 F., were produced. In September, some of the large papular lesions on the arms and legs became gummatous and ulcerated. She then presented papular squamous secondary lesions and late gummatous lesions in proximity.

Treatment has been continuous, consisting of the administration of arsphenamine, silver arsphenamine, bismuth, mercury and iodides. In July, a mild arsenical dermatitis developed. There was no improvement with bismuth, mercury and a milk preparation injected intramuscularly; therefore, a course of neoarsphenamine was started on October 12. There was definite improvement in the eruption; the ulcerations healed. New papular lesions continued to develop. The mucous membranes have remained clear; there have been no alopecia or constitutional symptoms. At present there are several grouped, infiltrated, flat, scaly, dull red papules on the face, arms, knees and left shoulder. Some are independent, discrete lesions, while others have appeared at the periphery of a pink, slightly infiltrated, involuting lesion. Scarring of the atrophic type has resulted from some of the lesions. The skin of the nose is more or less diffusely involved. On the flexor surface of the right arm and on the right knee there are partially involuted lesions.

The Wassermann test on June 2 gave a reaction of 2 plus and the Kahn test was negative. On December 3, the Wassermann reaction was 4 plus and the Kahn test 4 plus. Blood counts showed: 4,900,000 red cells, 7,600 white cells and 84 per cent hemoglobin; neutrophils, 59 per cent; large lymphocytes, 13 per cent, and small lymphocytes, 28 per cent. On July 20 the amount of cholesterol in the blood was 200 mg. Spinal puncture was refused.

Biopsy performed on July 13 showed marked thinning of the epidermis and parakeratosis in the central portion of the section. In some places there was acanthosis, while in others the epidermis was edematous and infiltrated by lymphocytes. In the papillary and subpapillary layers of the corium there was considerable edema, diffuse lymphocytic infiltration, and also some hyperplasia of the fixed tissues. There were a perivascular lymphocytic infiltration in the corium, no areas of necrosis and no giant cells. This case was presented for therapeutic suggestions.

DISCUSSION

Dr. Udo J. Wile, Ann Arbor: I think that Dr. Netherton wanted suggestions as to further therapy. It seems that the patient has resisted all forms of therapy that have been given, including arsphenamines, bismuth, iodine, mercury and proteins. I have seen one or two such cases of malignant syphilis, one of which has been reported. I do not think that the condition in this case is a malignant syphiloderm; I think that it is a resistant syphiloderm. I should advise an overwhelming injection of a single heavy metal preparation, for instance, 5 grains (0.324 Gm.) of mild mercurous chloride or 5 grains of mercuric salicylate. A heavy dose sometimes gives good results when no result is obtained with much smaller doses. In people in whom the condition is resistant to arsphenamine, treatment with heavy metal preparations will give better results.

Dr. Karl G. Zwick, Cincinnati: As a suggestion, I submit the thought that, besides building up the patient's general resistance, some form of fever therapy might prove useful, as Kyrle, Schamberg and others have shown its usefulness in early syphilis.

Dr. E. B. Tauber, Cincinnati: I agree with the diagnosis and wish to add a suggestion regarding therapy. Dr. Goldblatt of Cincinnati suggested the following therapy for patients who have become resistant to treatment with metal preparations: several treatments of sodium thiosulphate, 3 Gm. daily, are given before treatment with arsphenamine is begun, etc. He reports a number of cases in which success was obtained by this procedure.

DR. R. G. SENOUR, Cincinnati: As regards Dr. Tauber's suggestion, I have taken care of a number of patients for him, using fifteen doses of sodium thiosulphate followed by six weeks of treatment with protoiodide of mercury, with successful results.

DR. E. W. NETHERTON, Cleveland: Vaccine therapy was tried; typhoid vaccine was given intravenously, with three elevations of temperature. A few more doses might have been beneficial, but the patient did not show much improvement. Sodium thiosulphate was tried. I should like to try malaria, but I have not convinced the patient that she would be benefited by it. I shall try Dr. Wile's suggestion of a large injection of mild mercurous chloride.

NEW YORK DERMATOLOGICAL SOCIETY

EDWARD R. MALONEY, M.D., *Secretary*

Regular Meeting, Dec. 15, 1931

J. FRANK FRASER, M.D., *President*

ERYTHEMA PAPULATUM CIRCINATUM (DARIER). Presented by DR. F. C. COMBES.

C. C., a girl, aged 3 years, born in the United States, had an eruption of approximately six months' duration on both lower extremities. The family and personal histories were of no significance.

On both thighs and legs were several plaques of erythema with irregular festooned borders varying in diameter up to 10 cm. The plaques were brownish red, and the borders raised, rounded and cordlike. The outer margins of the borders were of brighter color, and the lesions were sharply defined. There were a few smaller lesions, particularly about the ankles, which were distinct, flattened nodules. The mother of the patient volunteered the information that all the lesions began as small papules. There were no scaling and no subjective symptoms. The lesions had gradually enlarged, and new lesions had appeared from time to time.

DISCUSSION

DR. BINFORD THRONE: I accept the diagnosis. I have seen twelve or fourteeen cases that belong in the general group of erytheme annulaire centrifuge. The condition in this case is of a type I have not seen personally, but I think it belongs in the group.

DR. HOWARD FOX: This case presents a most unusual clinical picture, with the solid patches of somewhat quadrangular shape and the distinctly elevated, firm border. We should all agree that it belongs in the group mentioned by Dr. Throne.

DR. GEORGE M. MACKEE: I cannot discuss the case along the lines mentioned by Dr. Fox, for I have not seen an identical one. One seldom sees two like cases of this condition. I recall one patient who had lesions like granuloma annulare. In some patients the condition continues in the same way for two or three years, and then ordinary erythema multiforme with bullous lesions develops.

DR. BINFORD THRONE: We had one case that showed an enormous amount of pigment. The lesions were more or less circular, but the pigment was more marked than in this instance. I read of a case in the *Bulletin de la Société française de dermatologie et de syphilologie* in which the patient showed a large amount of uric acid and responded to treatment with methenamine. Two of my patients who were treated with this drug showed good results; other patients showed no results whatever.

DR. F. C. COMBES: I presented the case because it was unusual. I have never seen another exactly like it. It is almost a replica of Darier's original case, which he described under the name érytheme papulo-circiné migrateur chronique. Other conditions approaching it in nature have been described as erythema figuratum perstans (Colcott Fox) and érythème annulaire centrifuge. I prefer Darier's original name, since the fundamental lesion, as shown about the child's ankle, is a flat papule and not erythema. McLachlan (*Brit. J. Dermat.* **43**:506 [Oct.] 1931) reported a case identical with this in a child of 2 years, except that it was a lesion of the cheek. The eruption started as a papule which gradually enlarged peripherally, the center becoming depressed, until a large plaque was formed. The border was raised, rounded and cordlike. Darier lays particular emphasis on the erythematous, highly colored outer edge of the border. The lesions in Darier's and McLachlan's cases were of much the same configuration as in this case, that is, angular, with a tendency to festooned or reniform lesions.

I shall have photographs made in this case and take sections from the lesions for histologic study. The patient is being treated with methanamine internally, as Dr. Throne has suggested.

A CASE FOR DIAGNOSIS (ULCERS OF THE LEG). Presented by DR. E. F. TRAUB.

J. R., a girl, aged 7 years, was born in New York City. The child's mother stated that her daughter had had a discharge of pus from the vagina about a year and a half before presentation, and again about six months prior to presentation. The exact nature or origin of the pus was not known, the mother believing it came from the kidney, whereas the history sounded as though it might have been due to vaginitis. The family history was negative for tuberculosis and syphilis. The child's grandmother, who had had a chronic cough and was underweight, had been living with the child's parents but had never had a pulmonary hemorrhage, nor had her condition ever been diagnosed as tuberculous.

The child's present trouble began with a "mosquito bite" about three months prior to presentation. The area was scratched vigorously, and small ulcers appeared at the site and in the immediate vicinity. The original lesion had increased a great deal in size until, as presented, it measured from 1 to 1½ inches (2.5 to 3.7 cm.) in diameter. The border was irregular, sloping in spots and undermined in others. The base, while fairly clean, was irregular and seemed to be made up of freely bleeding granulation tissue. In spite of local cleanliness and applications of ointment, the ulcers had been growing progressively worse. The Wassermann test was negative. Biopsy and a tuberculin test have not yet been performed.

DISCUSSION

DR. GEORGE M. MACKEE: I have seen a number of lesions exactly like those in this case and with exactly the same history; all of them occurred in children and adolescents. I was able to rule out syphilis, tuberculosis, drug eruption, and other condition. The final diagnosis was ecthyma or pyodermia. The lesions did not respond well to treatment, and they recurred in a few months. Some of the patients required rest in bed and applications of a very weak solution of sodium hypochlorite by the drip method. I suggest the possibility of pyodermia or ecthyma in this case.

DR. HOWARD FOX: The patient presents a clearcut picture of an ulcerating, gummatous syphilid. We all know, however, that a similar picture may be caused by tuberculosis. I presume no stigmas of congenital syphilis were found, and if this is so I should favor the diagnosis of tuberculosis.

DR. FRED WISE: In addition to the other investigative work, an examination for diphtheria bacilli would be indicated.

DR. E. F. TRAUB: The patient was seen yesterday for the first time and is presented simply for clinical discussion, as the only laboratory datum available was a negative Wassermann test. I was interested to hear Dr. MacKee say that

the term ecthyma may properly be applied to such a lesion, provided, of course, a specific infection can be ruled out. I have had several cases recently that presented much the same picture, and on careful study I was unable to find evidence of either tuberculosis or syphilis.

GRANULOMA ANNULARE OF EXTENSIVE DISTRIBUTION. Presented by DR. PAUL E. BECHET.

A. C., a boy, aged 6 years, had had for six months before presentation seven or eight ringed lesions scattered over the hands, feet, and body. The lesions consisted of deep-seated, firm, whitish nodules, arranged in ring formation. Several of the rings had undergone involution, leaving an irregular, crescentic outline. There were no subjective symptoms. A tuberculin test with a 1 : 10,000 dilution was negative.

A CASE FOR DIAGNOSIS (VESICULOPAPULAR DERMATITIS). Presented by DR. E. F. TRAUB.

M. E., a widow, aged 47, was born in New York. Her family history and past personal history were essentially negative, and she gave no history of any type of illness or drug taking before the appearance of the eruption for which she was presented. The lesions began on the arms and legs three weeks previous to presentation and about a week later spread to the body. The eruption began with tiny papules which became vesicular and were intensely pruritic; from scratching, the lesions became excoriated and covered with tiny crusts. There was nothing characteristic about the distribution. Scabies did not suggest itself as a likely diagnosis, and her husband, with whom she slept, was free from any itch. A specimen for biopsy had been taken of one of the lesions, but the report was not yet available, as the patient was seen for the first time on the preceding day.

DISCUSSION

DR. F. C. COMBES: I do not think the condition is scabies, that is, not human scabies; nor does it look much like prurigo. I should like to suggest the diagnosis of cat or dog scabies. I once saw a condition, in a woman, that looked very much like this. The early lesion is an irritable papule which is early capped by a vesicle. The distribution in this case also strongly suggests that diagnosis. The patient has a cat, and although she says there is no evidence of any skin disease, it probably had the disease. Cat scabies is often difficult to detect. The disease is not transferable between human beings, but occasionally is transmitted from cats and small lap dogs to man. The distribution in animals differs from that in man in that in animals it tends toward a more general distribution, particularly on the trunk and extensor surfaces of the extremities.

DR. E. F. TRAUB: But for the fact that the eruption is exceedingly pruritic, the picture suggests a type of condition which we have seen in numerous instances recently and which has been called parapsoriasis varioliformis acuta.

DR. HOWARD FOX: I do not see how one can make a diagnosis of papulonecrotic tuberculid in a case of three weeks' duration, which has not had time to produce scars, and which is intensely pruritic. All one can do at the present time is to call this a vesiculopapular dermatitis of unknown, possibly toxic, origin.

MILIA (UNUSUALLY EXTENSIVE DISTRIBUTION). Presented by DR. PAUL E. BECHET.

B. F., a woman, aged 57, stated that she first began to notice lesions five years before presentation; they had spread extensively since that time. She presented for examination innumerable typical milia, covering the entire neck, chest and upper part of the back.

CASES PREVIOUSLY PRESENTED

LICHEN PLANUS. Presented by DR. FRED WISE.

Dr. Wise reported on a case presented at the previous meeting with a diagnosis of lichen planus on the hands. The patient, a child of 7 years, had also impetigo of the face. There was one bullous lesion on the back of the hand. The histologic diagnosis was lichen planus bullosus.

A CASE FOR DIAGNOSIS. Presented by DR. BINFORD THRONE.

Dr. Throne reported on a case mentioned at the October meeting, that of a woman with an eruption of many years' duration. Dr. Wise had suggested that it might be an instance of colloid degeneration. The section was examined for that and proved negative.

DETROIT DERMATOLOGICAL SOCIETY

H. J. PARKHURST, M.D., *Reporter*

Regular Meeting, Dec. 15, 1931

CLAUD W. BEHN, M.D., *Presiding*

URTICARIA PIGMENTOSA. Presented by DR. CYRIL K. VALADE.

L. A., a woman, aged 23, a clerk, of Syrian descent, presented a generalized brownish macular eruption of five years' duration, only the hands and face being unaffected. There was mild pruritus, and friction produced wheal formation in the macules. Cutaneous tests showed sensitization to veal, pork and coffee. The Wassermann reaction was negative.

DISCUSSION

DR. ROBERT C. JAMIESON: Is this a case of urticaria pigmentosa or one of urticaria with pigmentation? Its onset was quite late.

DR. HOWARD J. PARKHURST: It seems to be the adult type of urticaria pigmentosa, for when the macules are stroked, wheals appear. I would suggest ultraviolet irradiation.

DR. CYRIL K. VALADE: Ultraviolet irradiation has been used, and improvement has followed.

PITYRIASIS ROSEA (ATYPICAL). Presented by DR. CYRIL K. VALADE.

J. B., a laborer, aged 34, born in Jugoslavia, presented a generalized eruption of four months' duration, with a predilection for the face, trunk, arms and legs. The lesions were mostly small or as large as a medium-sized coin, and consisted of faint erythematous macules and small papules; there were a few rings of minute vesicles, the centers being fawn-colored. On the elbows and knees there were a few small papules, each with an easily detached fine white scale. There was mild pruritus.

DISCUSSION

DR. ARTHUR E. SCHILLER: The eruption is of four months' duration. The lesions present more scaling than is usually seen in pityriasis rosea. Perhaps the condition is atypical psoriasis.

DR. GEORGE VAN RHEE: I felt that it was pityriasis rosea.

DR. ROBERT C. JAMIESON: It may be atypical pityriasis rosea or atypical psoriasis. There are lesions, here and there, almost typical of either disease. The appearance of the eruption may change after further observation.

Dr. Cyril K. Valade: At first I considered the condition psoriasis, but as the lesions gradually fade the eruption looks more like pityriasis rosea.

A Case for Diagnosis. Presented by Dr. Arthur E. Schiller, Dr. William G. Saunders and Dr. Clyde K. Hasley.

M. D., an American girl, aged 11, whose parents and older sister were living and well, had had an abundant growth of hair on the scalp at birth, but had lost it at the age of 5 years and again at the age of 10. There was a sparse regrowth of dry blond hair about 1 inch (2.54 cm.) in length.

When the patient was about 3 months old small blisters and crusts appeared behind the ears and on the buttocks, and at that time the eyelashes were lost. At the age of 2 years the eruption had disappeared, but it had soon returned. There were lesions in the axillae, in the decubital areas, in the groin and popliteal regions and quite generally distributed over the lower extremities and about the eyes, accompanied by pigmentation. Injury was said not to have produced blisters. There had been some pruritus, and the patient was highly neurotic. The appetite had never been good, and the diet had possibly been deficient at times. Attacks of diarrhea had occurred, and there had been intense sweating, chiefly nocturnal.

This case was presented before the Pittsburgh Dermatological Society, where diagnoses of epidermolysis bullosa hereditaria, pellagra and acrodynia were suggested.

DISCUSSION

Dr. Howard J. Parkhurst: Blisters have appeared at points subject to trauma, the nails have been lost, and there are scars on the tip of the tongue. Therefore I consider the condition epidermolysis bullosa hereditaria.

Dr. Cyril K. Valade: Apparently there is some congenital defect, manifested mentally and cutaneously.

Dr. Robert C. Jamieson: A year or so ago we had at Harper Hospital a case of congenital ectodermal defect similar to this. I agree with a diagnosis of epidermolysis bullosa hereditaria, and feel that other congenital defects may underlie the condition.

BRONX DERMATOLOGICAL SOCIETY

Theodore Rosenthal, M.D., *Secretary*

Regular Meeting, Dec. 17, 1931

Henry Silver, M.D., *President, in the Chair*

Lupus Erythematosus. Presented by Dr. Charles Greenhouse.

D. B., a girl, aged 18, presented a sharply defined, raised, red, macular lesion the size of a penny, in the center of the left cheek, and a similar lesion, pea-sized, above it which had persisted for the two years prior to presentation. A superficial crusted lesion on the forehead appeared the night before presentation. The patient had used salves. There was a scar on the right side of the neck most likely from tuberculous adenitis. This patient was a sister of E. B., who was also being treated for lupus erythematosus.

Microscopic examination showed throughout the cutis an interstitial and parenchymatous edema, more marked in the upper part. Here the vessels were markedly dilated, and the cellular infiltration was grouped chiefly around the follicles and the glands. The cellular infiltration was composed of lymphocytes and connective tissue cells. Just below the epidermis the fibers were separated in some places; the basal cell layer was wanting, and some of the cellular elements had wandered into this area. The epidermis was thinned and the granular layer

was present, but composed of only one layer of cells. The elastic tissue in the area of infiltration was entirely gone.

LUPUS ERYTHEMATOSUS. Presented by DR. CHARLES GREENHOUSE.

E. B., a man, aged 35, married, born in the United States, the brother of the patient previously presented, had been perfectly well until one year before presentation, when he was exposed to the sun and had applied vinegar to his face (to harden the skin). Soon after that an eruption began on his forehead, which spread to the rest of his face in the course of six months. The entire frontal portion of the scalp showed moderate erythema and slight atrophy. The eruption had a bat-wing distribution over his nose and cheeks, involving the entire surface of the cheeks and spreading to the chin and also behind the ears. There were characteristic redness, scaling and atrophy, with erythema of the chest and intrascapular area. The Wassermann reaction was negative. Biopsy confirmed the clinical diagnosis.

LUPUS ERYTHEMATOSUS. Presented by DR. GEORGE J. SPINNER.

M. H., a man, aged 43, white, married, with an unimportant family history, about ten weeks before presentation began to feel itching at the lower part of the nose on the left side. Thinking it was a pimple, he squeezed it, and the next morning noticed a red spot. He used a salve for two months without improvement. At presentation he had a round patch about 15 mm. in diameter typical of the fixed, circumscribed discoid type of lupus erythematosus. A gold and sodium thiosulphate preparation was given intravenously, 25 mg. as the initial dose. We propose to continue the treatment with increased doses of this chemical twice a week.

The Wassermann reaction of the blood was negative.

DISCUSSION

DR. CHARLES GREENHOUSE: The first two patients were treated with a gold and sodium thiosulphate preparation for a period without any noticeable improvement. Treatment was then instituted with bismuth intramuscularly and 10 per cent bismuth oxychloride locally, which resulted in improvement. The technic employed is in accordance with the work of McKenna in England, who claimed to have secured good results.

DR. L. CHARGIN: The patients presented by Dr. Greenhouse exhibit different types of lupus erythematosus. The brother presents the fixed type, while the sister shows the superficial type, without scaling and with very little atrophy. Patients with the type presented by the latter should not be treated too vigorously, since there may be progression into the subacute or acute type of the disease. Also they should not be exposed to sunlight, which may cause an extension of the process.

DR. MARION B. SULZBERGER (by invitation): This is a remarkable coincidence, as we know that there is usually no familial tendency in lupus erythematosus.

DR. A. ROSTENBERG: I have never seen two cases in one family before. Is there any tuberculous taint in the family?

DR. CHARLES GREENHOUSE: The occurrence in this brother and sister appears to be merely a coincidence. The only suggestion of tuberculosis is the fact that the girl has had cervical glands removed.

DR. C. LERNER: The lesion on the girl's face appeared raised and was undoubtedly subacute. It impressed me as being a sarcoid.

DR. I. LASHINSKY: I saw this patient when she was first admitted to the clinic. At the time, the lesion impressed me too as being a sarcoid, but now I am inclined to agree with the diagnosis of lupus erythematosus. Perhaps local therapy should be tried.

DR. S. FELDMAN: Results with local gold therapy in lupus erythematosus in my experience have not been good. I believe that the good results claimed for local injections have been due to the irritant action of the solution used. Any corrosive solution would produce a slough when injected into the lesions. I cannot see the rationale for local therapy in lupus erythematosus.

DR. F. A. DIASIO: The effect of gold therapy locally is to get rid of the edema. It has no caustic action.

DR. T. ROSENTHAL: My experience with local injections of a gold preparation is limited to one patient, a colored girl, who received a number of intradermal injections into the lesion without improvement.

DR. H. SILVER: I may state that Dr. Peck and I have tried locally an ointment containing gold and sodium thiosulphate in lupus erythematosus, without improvement.

DR. M. B. SULZBERGER: In considering the effect of various metals in lupus erythematosus, one must not jump to the conclusion that lupus erythematosus is tuberculous. Gold therapy will not cure patients with pulmonary tuberculosis, although it has been efficacious in some tuberculids. My experience in Zurich and Breslau with gold therapy has been very satisfactory, but other chemicals will sometimes act as well. The danger in the administration of a gold preparation is greater than with the arsphenamines. We have used silver arsphenamine instead of a gold preparation and then neoarsphenamine, with results approximately as good as those with gold therapy. It is probable that a great many metals have the same therapeutic effect.

DR. A. ROSTENBERG: All new remedies at first blush seem to be effective. I have found the concomitant use of carbon dioxide snow very useful in cases in which some of the lesions did not improve with gold therapy.

DR. I. LASHINSKY: From observations of cases in the Post Graduate Hospital I should say that about 50 per cent of cases clear up with gold therapy. Gold preparations should not be given if tuberculosis is present in the lungs. If after twenty injections, no improvement is seen, the treatment should be discontinued.

DR. V. MENDELSOHN (by invitation): Gold therapy seems to work better in white than in colored patients. In my experience local injections of a gold preparation have been worthless.

DR. L. CHARGIN: There is no doubt in my mind that the newer methods of treating patients with lupus erythematosus are vastly superior to the older ones. I believe that the results with gold therapy are better than with neoarsphenamine and silver arsphenamine. It would seem that some cases will respond to this type of therapy while others will not. I recently had a patient who had psoriasis and lupus erythematosus, and it is of note that both conditions improved with the gold therapy.

DR. E. KELLY: I recently had a very unpleasant experience with gold therapy. After three injections of a gold preparation, the patient became acutely ill, and what appeared to be pulmonary tuberculosis developed. After a stormy course the signs in the chest disappeared, and the patient became well again. The cutaneous condition also disappeared.

DR. G. J. SPINNER: My results with gold therapy have also been poor. Some months ago, I observed a severe toxic reaction with a fatal termination in a child following gold therapy.

RECURRENT BASAL CELL EPITHELIOMA. Presented by DR. HENRY SILVER.

E. W., a woman, aged 26, born in the United States, is the mother of a healthy girl. In 1926, she noticed a growth about the size of a pea in the middle of the forehead. She consulted a dermatologist who diagnosed the lesion as epithelioma and advised roentgen treatment. The patient submitted to the treatment, and

the lesion disappeared. When I saw her in 1928, she presented an irregular, soft, slightly depressed scar in the middle of the forehead near the hairline, the size of a nickel. About nine months before presentation, she noticed a small reddish area in the center of the scar, which became crusted. The border of the lesion was slightly elevated, and the center was covered with a grayish crust. On removal of the crust, a moist area became visible. In a period of four weeks the lesion grew from the size of a pea to that of a nickel. The lesion was destroyed by electrocoagulation, and after the area healed, radium was applied. She received 250 mg. hours at 1 cm. distance from the lesion, filtered through 1 mm. of lead. The area cleared up entirely, but three months later the lesion reappeared.

DISCUSSION

DR. A. ROSTENBERG: After so many recurrences, I should advise wide and thorough excision.

DR. M. B. SULZBERGER: It seems to me that the scar is attached to the bone. I believe that a radical excision including the bone, followed by skin graft, would be the best plan of therapy.

DR. L. CHARGIN: I should strongly suggest a histologic reexamination; then a thorough curettage of the area should be done.

DR. C. LERNER: About 90 per cent of epitheliomas of this region are of the basal cell type. This lesion may not be a recurrence of a basal cell epithelioma. There seems to be no attachment to the bone. The crust and underlying appearance suggest that we may be dealing with a sebaceous lesion.

DR. H. SILVER: The point made by Dr. Lerner, that there is no attachment to the bone, is well taken. The involved area, though deeply scarred, is freely movable. Wide excision and plastic repair are of course the last resort.

A CASE FOR DIAGNOSIS (LICHEN PLANUS OR LEUKOPLAKIA ORIS). Presented by DR. MAURICE UMANSKY.

A man, aged 33, a salesman, first noticed the eruption in the mouth about ten years before presentation. On examination he presented solid white patches on the mucosa of the cheeks, bilaterally along the interdental cleft and ending at the commissures of the mouth. The subjective symptoms were slight, an occasional burning sensation, especially when he took spicy food. The patient used to be a heavy smoker of cigars and cigarets. In the last two years he had smoked less, and there was some improvement. The patient wore a removable bridge which did not cause any irritation. He did not have syphilis.

DISCUSSION

DR. L. CHARGIN: I believe that this is a case of lichen planus. At the inner sides of the labial commissures the appearance is that of the leukoplakia observed in syphilis, but the annular appearance of the lesions on the cheeks leads me to believe that it is lichen planus.

DR. C. LERNER: My diagnosis is leukoplakia.

DR. M. UMANSKY: There are streaks and ring formations on the buccal mucosa. The patient is a heavy smoker and wears a dental plate. There is no evidence of lichen planus lesions on the body. The most likely diagnosis is leukoplakia.

A CASE FOR DIAGNOSIS (UNUSUAL PIGMENTATION). Presented by DR. HARRY B. FEILER.

B. M., a boy, aged 12½ years, came to the clinic with an eruption on the right side of the neck extending to the shoulder. A diagnosis of bullous impetigo was made, and the patient received 5 per cent of white precipitate ointment. Two

weeks later he presented himself again with the original condition cleared up, and in place of this, however, a secondary dermatitis. This improved with calamine lotion. Six weeks later the patient again returned with an entirely new eruption on the right side of the neck, extending to the shoulder and to the anterior aspect of each shoulder joint. This consisted of bluish pigmentation, somewhat resembling a purpuric eruption. The blood count was: hemoglobin, 76 per cent; erythrocytes, 3,960,000; leukocytes, 7,400; polymorphonuclears, 73 per cent; lymphocytes, 24 per cent; monocytes, 3 per cent, and platelets, 170,000.

Because it was suspected that the pigmentation might be on the basis of a mercury dermatitis, a patch test was done with 1:5,000 mercuric bichloride and later with 10 per cent of white precipitate ointment. The reactions to both tests were positive, but no pigmentation had as yet developed. Since the eruption appeared, it had faded slightly. The mother claimed that when the patient exposed himself to cold the eruption was of a deeper color.

DISCUSSION

DR. M. B. SULZBERGER: This is a most interesting case. I cannot make a diagnosis at present. The pigmentation does not look like a hemosiderin or blood pigmentation, but like a hyperpigmentation with a melanotic pigment. The bizarre outline and configuration do not resemble any dermatoses with which I am familiar. Some parts resemble the condition known as incontinentia pigmenti. I suggest histologic study with the dopa reaction or a silver nitrate impregnation for pigmentation. If this were incontinentia pigmenti, one would expect to find little or no pigment in the epidermis and considerable pigment in the chromatophores of the cutis. I do not believe that there is any connection between this hyperpigmentation and the ammoniated mercury irritation or the impetigo. The shapes of the hyperpigmentated areas are too bizarre to allow this interpretation.

DR. S. FELDMAN: The eruption had the distribution of a bathing suit. I believe that this patient had dermatitis following sunburn.

DR. C. LERNER: A biopsy is important in this case to determine the location of the pigment. The endocrine status of the patient should also be investigated, as the boy appeared to have a Fröhlich syndrome.

DR. L. CHARGIN: This case is presented for diagnosis because of the unusual color of the pigmentation. The condition resembles very much maculae coeruleae, but is in an unusual location and phthirii were not found. I do not think that we are dealing with a pigmentation following a mercury dermatitis.

DERMATOPHYTOSIS AND DERMATOPHYTID. Presented by DR. ISIDOR MOGIL.

A girl, aged 10, presented a definite dermatophytosis of the feet and, in addition, a generalized eruption of two months' duration. This consisted of small, ring-shaped lesions with clear centers on the arms and a diffuse red papular eruption over the trunk. There was marked itching. The patient had received no treatment thus far.

DISCUSSION

There was general agreement with the diagnosis.

PAPULONECROTIC TUBERCULIDS AND LICHEN SCROFULOSORUM. Presented by DR. THEODORE ROSENTHAL.

J. H., colored, aged 14 years, born in the United States, had a definite tuberculous history. A roentgenogram of the chest showed old and fresh tuberculous lesions of the lung. In September, 1931, glands were removed from the neck, and the biopsy revealed tuberculous changes.

The present eruption began about seven or eight weeks prior to presentation, when the patient noticed a few pimples on the outer sides of both upper extremities. The eruption spread so as to involve the axillae and flanks.

The patient presented on the arms, axillae and flanks numerous papular, erythematous lesions ranging in size from 1 to 5 mm. in diameter, some of which had necrotic caps. In both epigastric regions were groups of smaller, skin-colored lesions with smooth, level tops. Numerous comedones and small pustules were present on the forehead and cheeks. The scar on the neck was the location from which were removed the tuberculous glands. Urinalysis, examination of the sputum and the Wassermann test gave negative results. Examination of the blood showed: hemoglobin, 73 per cent; red blood cells, 4,500,000; white blood cells, 11,200; polymorphonuclears, 42 per cent, and small lymphocytes, 49 per cent. There was a positive delayed reaction to staphylococcus toxin, 1:10, and a positive reaction to old tuberculin, 1:1,000.

DISCUSSION

DR. M. B. SULZBERGER: This patient presents not only the two types of lesions stated, but transitional forms between the two. The focal reaction following the administration of tuberculin is indeed interesting. It is also interesting to speculate whether the lesions on the forehead are of the same origin. They look clinically like acne vulgaris. I would suggest a Moro test and inoculation of material from these lesions into guinea-pigs. A diagnosis of papulonecrotic tuberculids cannot be based on histology alone, because almost all embolic phenomena involving the venous plexus in the skin or subcutaneous tissues give similar pictures. The diagnosis of tuberculids is usually based on one or more of the following points: (1) an association with tuberculosis elsewhere in the body, (2) hypersensitive or anergic (hyposensitive) tuberculin reaction, (3) positive Moro reaction, (4) finding of tubercles on histologic examination, (5) culture of the tubercle bacillus, (6) demonstration of the tubercle bacillus in the section and (7) positive results of inoculation into guinea-pigs.

DR. I. LASHINSKY: The lesions on the face resemble lupus miliaris disseminatus.

DR. L. CHARGIN: There is no question that the lesions are tuberculous. The lesions on the face, although they are follicular, do not conform to the picture of lupus miliaris disseminatus. While the lesions on the body closely resemble lichen scrofulosorum, those on the arms are not typical of the usual type of papulonecrotic tuberculids. They lack the typical development, the crusts and the typical scars.

DR. A. ROSTENBERG: The papulonecrotic lesions seem to predominate in the picture tonight, whereas a week ago there were numerous lichenified lesions grouped in the typical manner. I should like to inquire as to the therapy in this case and whether gold therapy would be indicated here?

DR. T. ROSENTHAL: I am gratified to hear this case elicit such an interesting discussion. It is true that tonight the papular lichenified lesions are not much in evidence, and that many of the papulonecrotic lesions have assumed a moist, pustular appearance. This I regard as due to the markedly positive tuberculin reaction. Biopsies were made of the various types of lesions and will be reported on at the next meeting.

ACRODERMATITIS CHRONICA ATROPHICANS AND MACULAR ATROPHY. Presented by DR. HENRY SILVER.

Mrs. R. S., aged 36, born in Italy, married, had no children, and aside from one miscarriage her personal history was negative. About one year before presentation she noticed a redness of her arms and legs, which had persisted. On examination she presented a diffuse redness of the forearms and arms, more marked on the extensor surfaces. The legs up to the region of the hips had the same erythematous aspect. The skin was thinned and cigaret paper-like. Above the left elbow there was a quarter-sized, sharply defined, depressed, wrinkled atrophic area within the diffusely erythematous region. Repeated Wassermann tests gave negative results.

DISCUSSION

DR. M. B. SULZBERGER: I have never seen this combination before. It is unusual to find macular atrophy within areas of acrodermatitis chronica atrophicans.

DR. H. SILVER: Jessner, in his study of acrodermatitis chronica atrophicans, reported a number of cases (twenty-three) in which this combination occurred. In our study on macular atrophy (Chargin, L., and Silver, H.: Macular Atrophy of the Skin, ARCH. DERMAT. & SYPH. **24**:614 [Oct.] 1931), a similar number of cases were collected, which would suggest that the occurrence is not infrequent. This mixed type of atrophy is also interesting from the standpoint of a common etiology.

BROOKLYN DERMATOLOGICAL SOCIETY

A. M. PERSKY, M.D., *Secretary*

Dec. 21, 1931

B. B. BERKOWITZ, M.D., *Presiding*

A CASE FOR DIAGNOSIS (MYCOSIS FUNGOIDES?). Presented by DR. G. PRICE.

P. K., a man aged 39, was admitted to the Coney Island Hospital complaining of a swelling on the dorsal surface of the right forearm of two months' duration. It was red, painful and fluctuating. A diagnosis of carbuncle of the right forearm was made. On Oct. 26, 1931, a 1 inch (5 cm.) incision was made through the skin into the tumor mass. It was found to be of a fibrotic nature. It was then removed in toto. The pathologic report on the specimen was chronic suppurative inflammatory reaction with polymorphonuclear and small round cell infiltration of the cutis and subcutis. The laboratory findings were all negative.

The patient signed a release on November 2, and was attended in the clinic for one week, at which time the wound broke down and a generalized erythematous eruption developed, consisting of nodules varying in size from that of a split pea to that of a small walnut. The eruption was nonpruritic, nonsuppurative and without scales. Later, small pustulovesicles appeared in the center of some of the lesions, especially those on the forehead. Some of the lesions were elongated. The area around the wound broke down, suppurated and became gangrenous, with a ridge dividing the ulcerated area into two parts, one slough coming away easily, the other remaining adherent. The border was raised, prominent and roughened. The base was always seropurulent.

On December 18, a papular lesion developed, with an inflammatory areola on the hard palate. The patient had been readmitted to the Hospital on November 16. Results of cultures of the blood and nasal secretions and of examinations of the pus were all negative.

On November 25, the biopsy report read: The skin nodule reveals a dense, infiltrative lesion of the subcutaneous region composed of mononuclear cells of the lymphoid type. These cells are quite uniform in size. There is no perivascular arrangement. This arrangement is also found about the hair follicles and sweat glands, and the same pathologic process was found in a specimen taken from the wound for biopsy. A restudy of the tumor originally excised showed a similar lesion. A diagnosis of mycosis fungoides was suggested, although the lymphosarcomatous form of the lymphoblastoma group is to be seriously considered.

DISCUSSION

DR. L. CHARGIN: I had occasion to see this case about two weeks before presentation at another meeting, but I did not discuss it then, because I was in doubt at the time as to a definite diagnosis. The picture is, however, quite clear this evening. The process began with a large infiltrating mass, which was

incised in the mistaken idea that it was an infection. Subsequently, there developed a generalized, flat, erythematous eruption not palpably infiltrated. A clinical diagnosis was quite difficult at this time. The lesions have now become markedly infiltrated and consist of elastic tumors with reddish and reddish-blue coloration. Many are ulcerated. The condition is now quite definitely mycosis fungoides of the d'emblé variety.

The pathologic process as presented is not characteristic of mycosis fungoides. I would suggest that further study be made or that another specimen of tissue be taken for biopsy. I would also suggest further therapy with arsenic and the roentgen rays.

DARIER'S DISEASE. Presented by DR. A. WALZER.

F. F., a married woman aged 29, had had the present trouble for fifteen years. It began on the forehead and gradually spread. During the summer months it would improve. She had been to many clinics, and had been presented before a number of organizations. She had received various treatments: ultraviolet irradiation, injections, local applications, etc.

On presentation, she exhibited a hyperkeratosis around the follicles, which gradually increased in size and became very greasy looking and brown. The papules varied in size and were surmounted by a central concretion. In some locations, especially the shoulders, they coalesced and formed a rough papillomatous patch. The lesions were located on the forehead, across the eyelids, ears neck and shoulders and between and under the breasts. Around the upper lip, mouth and chin, the lesions formed an erythematous patch almost like seborrhea. The scalp was covered with thick white adherent scales. A peculiar odor was associated with the lesions.

DISCUSSION

DR. L. CHARGIN: This case is exceedingly interesting. I agree with Dr. Walzer in his diagnosis of Darier's disease. The characteristic lesions are present on the face and trunk, but the lesions on the scalp are seborrheic and are not those of Darier's disease. The patient states that the eruption on the scalp clears up from time to time. Darier's disease does not do this. We are dealing with Darier's disease associated with seborrhea. This combination is well known.

DR. A. WALZER: There is not much more to say in this case, but the appearance of seborrheic patches on the scalp is so common in a clinical picture of Darier's disease that one may readily say that they go hand in hand.

This case was presented before the Academy of Medicine, but I could find no record of the discussion.

GENERALIZED NEVUS. Presented by DR. A. WALZER.

C. K., a girl aged 15 months, had had no eruption on the skin until about ten months previous to presentation, when the mother had noticed the first spots on the elbows and knees. Gradually they spread until they involved the entire body.

On presentation, there were small, brownish, flat, pigmentary patches scattered over the entire body. Some were discrete papules, a few in linear arrangement and others in patches of various sizes and shapes. Around the malleolar regions and elbows, the lesions were somewhat keratotic. Dermographism was pronounced. The child was otherwise apparently normal.

Book Reviews

Studien über die Veränderungen der Nachgeburt bei Lues. By T. E. Olin. Pp. 165, with 20 illustrations. Jena: Gustav Fischer, 1931.

This monograph is a reprint of the last number of volume 6 of a series of studies from the Pathological Institute of the University of Helsingfors, Finland. It begins with a review of the literature covering twelve pages. Then follows a short statement of the author's choice of patients and the technic of his investigation, which consumed three years and included thirty-nine syphilitic pregnancies, twenty-one nonsyphilitic controls and records of a thousand births during the year 1930. Among these were eleven additional cases of syphilis. The problem was to determine which of the anatomic pathologic changes in the afterbirth can be reliably ascribed to syphilis and used as diagnostic signs. At the same time Olin studied the effect of antisyphilitic treatment of the mother on the changes in the afterbirth.

His material was divided into three groups: Those who were infected before conception and had received treatment, those who were infected at or after conception and received treatment and those who received no treatment. There were thirteen cases in the first, eleven in the second and fifteen in the third group. The clinical features of the various cases are then discussed, including the length of the infection of the mother, the fate of the child, etc. Eleven pages are then devoted to the macroscopic changes in the afterbirth. The next fifty-four pages contain the principal part of the monograph, a discussion of the microscopic changes in the various parts of the afterbirth. The relation of these changes to infection in the fetus is discussed, and then the relation of the changes one to another and to the treatment received by the mother.

Olin's conclusions disagree to a marked degree with the teaching in textbooks. He rejects the placenta—child weight ratio, stating that for Finland, at least, the quotient 1:6 is entirely unsuitable. Likewise, the relation of the weight of the afterbirth to the length of the child born alive or dying during birth is not abnormal in syphilitic patients. The average weight of the afterbirth of syphilitic mothers does not exceed the normal, if the birth is at the normal period.

Histologically, certain changes are common in syphilitic patients and less common in nonsyphilitic patients, and can therefore be looked on as probably syphilitic, especially if they are marked. The discovery of Spirochaeta pallida is the only sure criterion, however.

Antisyphilitic treatment of the mother during pregnancy prevents the onset or delays the development of these changes to a large degree.

Finally, eleven pages are devoted to a bibliography.

This treatise impresses one that the work has been honestly and intelligently done, and that the conclusions are justified by the results. It is a valuable contribution.

Rational Pharmaceutical Treatment of Common Skin Diseases. By Herman Goodman. Price, $10. Pp. 350, with 72 illustrations. New York: Medical Lay Press, 1932.

Goodman attempts something unusual in that he limits himself to a consideration of the treatment of only the cutaneous diseases most commonly encountered: eczema, tinea, acne, scabies, psoriasis, seborrhea, impetigo, urticaria, dermatitis venenata, alopecia, pediculosis, pruritus and verrucae, in the order named. The 350 pages of text include, in addition to outlines of treatment, four chapters on the principles of dermatology, a chapter on the life cycles of animal parasites of the human skin, lists of diets, prescription formulas and clinical descriptions

of the diseases. The book contains much information that is useful and some statements that will not meet with general approval. The section on bathing and soaps, as well as the paragraphs on the preparation of ointments and lotions, should be useful to the practitioner. But when, in the treatment of juvenile acne, the author includes instruction in sex hygiene and discusses the true facts of adolescence to both boys and girls, in the reviewer's opinion, he is without the bounds of propriety, nor does he make clear how this helps control the acne. For ringworm of the toes he recommends highly the use of ultraviolet radiation as a routine treatment, and he says that people who have much perspiration of the feet apparently have less tendency to have a relapse. This, of course, has not been the experience of most observers, nor can we agree with his opinion that the popularity of Whitfield ointment is due to some curious accident. The chapter on pruritus is inadequate. Instead of a workable classification, there is an alphabetic list of the conditions that may be associated with itching — from suprarenal disease through constipation, idiosyncrasy and pyorrhea alveolaris to zoster.

The format of the book lacks balance; for instance, eight pages are devoted to dermatitis venenata, three and one-half of these to rhus, and ten pages are devoted to the treatment of pediculosis. The type and illustrations are excellent and the book is well printed, but the author's style of short choppy sentences makes reading difficult.

In general, the treatment is practical, as the methods outlined are obviously those used by the author, but he offers little that is not contained in the recent standard textbooks.

Die Wassermannsche Reaktion in ihrer Bedeutung für die spezielle Pathologie und Therapie der Syphilis. By August Poehlmann, Professor and Chief of Dermatology, University Polyclinic, Munich. Price, 8.40 marks. Pp. 170. Munich: Rudolph Müller & Steinicke, 1931.

This is a 170 page monograph, which thoroughly covers the subject matter indicated by the title. The work is based on a study of 180,000 tests, with occasional case citations and frequent references to the work of other investigators. There is appended a full bibliography. The first chapter deals with specificity, elaborating on the disorders and circumstances in which nonspecific positive reactions may be obtained, and emphasizes the importance of proper interpretation of reactions and of careful technic. There is then a consideration of the character of the reactions and their significance in the various stages and manifestations of syphilis. The author does not favor the unscientific grouping, for therapeutic purposes, of seronegative and seropositive cases. The significance of changes in the spinal fluid in all stages and phases of syphilis is also taken up, and in the consideration of tertiary syphilis, the variability of the Wassermann reaction, when different tissues or organs are involved, is fully discussed. The subject of maternal syphilis and the serodiagnosis of congenital syphilis are especially well presented. The influence of treatment on the Wassermann reaction is discussed from the standpoint of the individual drugs employed in treatment, as well as from observations on combined therapy. The closing chapters deal with the rôle of the Wassermann reaction in determining the fundamental basis of syphilis management and the prognostic interpretation of reactions.

The text is not so much an analysis and interpretation of a large series of Wassermann reactions as it is a readable and scientifically accurate presentation of the clinical importance of the Wassermann test. The value of this monograph to every one engaged in the treatment, teaching or investigation of syphilis cannot be overemphasized.

CORRECTION

In the article, "A Case of Xeroderma Pigmentosum," by Drs. Becker, Pautrier and Woringer, in the May issue of the ARCHIVES (**25**:915, 1932), "phagocytic melanoblasts" in the legend for figure 4 should read "phagocytic chromatophores."

Directory of Dermatologic Societies *

FOREIGN

Royal Society of Medicine, Section of Dermatology

President: A. M. H. Gray, 30 New Cavendish St., W. 1, London.
Secretary: H. Thompson Barron, 53 Queen Anne St., W. 1, London.

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

George Miller MacKee, Chairman, 200 W. 59th St., New York.
Francis E. Senear, Secretary, 55 E. Washington St., Chicago.
Place: Milwaukee. Time: 1933.

American Dermatological Association

W. H. Mook, President, 3720 Washington Blvd., St. Louis.
W. H. Guy, Secretary, 7026 Jenkins Arcade, Pittsburgh.
Place: Chicago. Time: 1933.

British Association of Dermatology and Syphilology (Canadian Branch)

Philip Burnett, President, 2 Simpson St., Montreal.
L. P. Ereaux, Secretary, 1380 Sherbrooke West, Montreal.
Place: Toronto. Time: June 24, 1932.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Lee McCarthy, President, 1835 Eye St. N. W., Washington, D. C.
M. H. Goodman, Secretary, 401 Medical Arts Bldg., Baltimore.

Central States Dermatological Association

Howard J. Parkhurst, President, 316 Michigan St., Toledo, Ohio.
Robert E. Barney, Secretary, 1021 Prospect Ave., Cleveland.
Place: Pittsburgh. Time: October, 1932.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City, Iowa.
Robert E. Jameson, Secretary, 201 West Second St., Davenport, Iowa.

New England Dermatological Society

Arthur M. Greenwood, President, 416 Marlboro St., Boston.
William P. Boardman, Secretary, 388 Marlboro St., Boston.

Southern Medical Association, Section on Dermatology

Emmet R. Hall, Chairman, 1001 Exchange Bldg., Memphis, Tenn.
Dudley C. Smith, Secretary, University, Va.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
Frank Wilson, Secretary, 310 Greenleaf & Crosby Bldg., Jacksonville, Fla.
Place: Jacksonville, Tampa, Miami and place of meeting of state medical society.
Time: Quarterly.

Louisiana Dermatological Society

R. A. Oriol, President, 921 Canal St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 150 Baronne St., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Edward R. Maloney, Chairman, 853 7th Ave., New York.
George C. Andrews, Secretary, 115 E. 61st St., New York.

Medical Society of the State of Pennsylvania Section on Dermatology

Edward F. Corson, President, Medical Arts Bldg., Philadelphia.
Stanley Crawford, Secretary, 200, 9th St., Pittsburgh.

Michigan State Medical Society, Section on Dermatology and Syphilology

Cyril K. Valade, Chairman, 1604 Eaton Tower, Detroit.
George H. Belote, Secretary, University Hospital, Ann Arbor.

Minnesota Dermatological Society

H. N. Klein, President, 350 St. Peter St., St. Paul.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.

Oklahoma Dermatological Association

C. J. Woods, President, 108 W. 6th St., Tulsa.
C. L. Brundage, Secretary, 616 Medical Arts Bldg., Oklahoma City.

Texas Dermatological Society

N. Riley Jackson, President, 110 W. 7th St., Austin.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Henry Silver, Chairman, 290 West End Ave., New York.
Theodore Rosenthal, Secretary-Treasurer, 115 W. 86th St., New York.

Brooklyn Dermatological Society

B. B. Berkowitz, President, 225 Eastern Parkway, Brooklyn.
A. M. Persky, Secretary, 1750 Ocean Pkwy., Brooklyn.

Chicago Dermatological Society

Michael Ebert, President, 25 E. Washington St., Chicago.
E. A. Oliver, Secretary, 55 E. Washington St., Chicago.

Cincinnati Dermatological Society

H. Jerry Lavender, President, 716 Provident Bank Bldg., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

Howard J. Parkhurst, President, 316 Michigan St., Toledo.
Robert E. Barney, Secretary, 1021 Prospect Ave., Cleveland.

Detroit Dermatological Society

Claud W. Behn, President, 1546 David Whitney Bldg., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

Irving R. Bancroft, Chairman, 412 W. 6th St., Los Angeles.
Chris R. Halloran, Secretary, 1052 W. 6th St., Los Angeles.

Manhattan Dermatologic Society

Fred Wise, Chairman, 200 West Fifty-Ninth St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

J. F. Burgess, President, Drummond Medical Bldg., Montreal, Canada.
B. Usher, Secretary-Treasurer, Medical Arts Bldg., Sherbrooke St., W., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Joseph J. Eller, Chairman, 100 W. 59th St., New York.
Leo Spiegel, Secretary, 241 W. 100th St., New York.

New York Dermatological Society

John Frank Fraser, President, 100 W. 59th St., New York.
Edward R. Maloney, Secretary, 853 7th Ave., New York.

Philadelphia Dermatological Society

Jacob M. Schildkraut, Chairman, 170 W. State St., Trenton, N. J.
Jacques P. Guequierre, Secretary, 1930 Chestnut St., Philadelphia.

Pittsburgh Dermatological Society

J. H. Fiscus, Chairman, 121 N. Main St., Greensburg, Pa.
Claude B. Norris, Secretary, 244 Lincoln Ave., Youngstown, Ohio.
Place: Pittsburgh. Time: October, 1932.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

Charles Schoff, President, 1127, 11th St., Sacramento, Calif.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

Index to Current Literature

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